ELEMENTARY PATHOLOGICAL HISTOLOGY

BARNARD

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To Norman Ashton.

Best wishes from
P. B. Illson

Christmas 1933.

ELEMENTARY PATHOLOGICAL HISTOLOGY

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BY

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WITH ONE HUNDRED AND SEVENTY-SIX ILLUSTRATIONS
ON FIFTY-TWO PLATES

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THIS BOOK IS RESPECTFULLY DEDICATED

TO MY FORMER TEACHER AND CHIEF

PROFESSOR HUBERT M. TURNBULL,

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DIRECTOR OF THE INSTITUTE OF PATHOLOGY,

THE LONDON HOSPITAL

PREFACE

ALL students of pathology know Virchow's text " omnis cellula e cellula," a few of them may have heard Bishop Hall's " God sells knowledge for sweat " : they generally take as little notice of one as the other. The object of the study of morbid histology is not to enable us to take a look down the microscope and say " tubercle " or " sarcoma " or " G.O.K." as the case may be, but to analyse the changes which are visible in individual cells and in the intercellular substances and by legitimate processes of deduction and experience to add them up into a coherent account of what has been happening in the tissue. Pathology is concerned with processes, not with states, and generally with what the body does to correct or evade the consequences of injuries. In the post-mortem room hypertrophied hearts and granular kidneys and nutmeg livers are of moment not as objects in themselves but as evidence of what has been going on in the body as a whole. We are no longer content to look at a dead body and be satisfied with " dropsy " or " cachexia " as a cause of death : we dissect it and try to put two and two together, though to be sure it is often enough that we cannot do the sum because we are not quite sure what the numbers really are. The same dissection and analysis and inference must be carried out under the microscope if we are to hope to understand even a little of what pathological histology has to teach us, and any section must be resolved into the various cells and particles and substances of which it may be compounded. In short, sections have to be looked at. The immersion lens is often discarded when bacteriology is finished with, but there is nothing inherently indelicate in a curiosity which brings it to bear on a tumour or inflammation, and it is only by such minute examination that we can expect to be in a position to explain the series of happenings which have led up to what we see and to guess with reasonable certainty what their effect on function has been and what they would have led to in the future if their development had not been interrupted by formalin and the microtome.

It gives me great pleasure to acknowledge my indebtedness to numerous students and pathologists for conscious and unconscious help in the preparation of this book, and particularly to my chief, Professor A. E. Boycott, for his encouragement and constructive criticism, and to Dr. H. D. Wright for help with the proof reading.

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ELEMENTARY PATHOLOGICAL HISTOLOGY

Inflammation

AS far as its histology is concerned inflammation consists of a progression of events following on injury to living tissue. The progressive nature of the reaction needs emphasis, because single sections can only show the stage reached at the moment of fixation. An ideal way of illustrating inflammation would be by means of a cinematograph film ; until that can be done it must be remembered that a section is comparable to a single photograph taken from the very many which would go to make up the whole.

The reaction is shown by changes in the tissue which is the seat of the injury, the connective tissues, the blood-vessels and the blood. Most epithelium plays a passive part until the stage of repair is reached, when that which covers surfaces has a considerable capacity for proliferation and can effectively re-cover wide areas. The epithelium forming glandular organs has a more limited power of proliferation, and unless the frame-work of the gland survives the regenerated part will not reproduce perfect gland. The connective tissues, blood-vessels and blood play the most active part in inflammation.

In addition to the fixed supporting binding and cementing elements of the connective tissues there are cells which when stimulated become free wandering cells ; these are histiocytes, and include macrophages, clasmatocytes, endothelial leucocytes, endothelioid cells, fat granule cells and other similar cells. All of them have, in common, the following characteristics : they are produced *in situ* by connective tissue, including endothelium and lymphocytes ; they are larger than leucocytes ; they have a relative abundance of protoplasm, and they are phagocytic.

At a very early stage in acute inflammation arterioles and small veins become dilated, and vessels which in the resting condition are not conspicuous become engorged ; from the vessels plasma and cells pass into the inflammatory focus.

The cells consist of leucocytes and red cells, and the proportion in which they appear in the reactions is very variable. The plasma, if it gets into a space or on a surface, most frequently becomes coagulated, forming irregular masses or columns of structureless non-nucleated material or a net-work in the meshes of which the cells appear to be caught. At the same time histiocytes become active and multiply in the inflammatory focus.

The reaction may be successful in neutralising or removing the damaging agent and the inflammation subside, the tissue being restored to its normal appearance. In many cases healing is less perfect, the inflammation terminating with the formation of scar tissue. This is brought about by the gradual autolysis and resorption of the inflammatory exudate, often assisted by histiocytes which injest and remove debris of all kinds, and the ingrowth of fibroblasts and capillaries. The fibroblasts lay down new fibrous tissue which becomes progressively more dense and the capillaries become closed ; it is this avascular dense fibrous tissue which is called scar tissue. If this process occurs on a surface such as pleura or peritoneum the scar tissue takes the form of fibrous adhesions between the visceral and parietal layers, and these persist after all other evidence of inflammation has disappeared.

The cause of the injury is not apparent in sections of all inflammation, though in many micro-organisms or other foreign bodies may be identified ; and although the tissues of the body do not react with the precision of chemicals in a test-tube, many of the bacteria excite a sufficiently specific reaction to suggest the cause. This is particularly true of the granulomatous inflammations and typhoid, which can be recognised with tolerable certainty, though the bacteria may not be seen, and to a less extent it is true of many of the purulent inflammations.

In a section of an inflammation we look for :

(1) Cause—bacteria, foreign body, products of autolysis of killed tissue.
(2) Injured or dead cells.
(3) Exudation of—
    Leucocytes.
    Red blood-cells (accidental).
    Plasma which commonly clots, particularly when it accumulates in a space (pleura or pericardium) or on a free surface (scab) —not so obvious in solid tissues.
(4) Repair by—
    (*a*) Histiocytes and leucocytes clearing up debris.
    (*b*) Fibroblasts and new capillaries.

FIG. 1.—A diagram of cells depicted in the succeeding examples of inflammation arranged in groups according to their kind.

Many of the polymorphs have a distinct cell outline and well-formed multilobed nucleus, the remainder are in various stages of dissolution.

The protoplasm of the eosinophils is full of coarse granules, and their nuclei are round, bilobed or multilobed.

The histiocytes vary greatly in size : the smaller are from a reaction in the alveoli of a lung, the larger are also from a lung and from a pericarditis, those forming the bottom row are from typhoid ; a group on the right contain blood pigment, and the cells next to them with vacuolated protoplasm contain fat ; two multinucleate giant cells are also shown.

The scanty protoplasm and deeply stained nuclei of the lymphocytes and the shape of cell and characteristic nucleus of plasma cells can be seen.

Fibroblasts have been drawn in various forms ; those with vacuolated protoplasm are undergoing mitosis.

FIG. 2.—A medium-power view of purulent meningitis. Many polymorphs are well formed, having clear-cut lobed nuclei and distinct cell outlines ; many others are degenerate, being represented by ill-defined bodies with ghost-like, fragmented or very deeply stained nuclei. Amongst the polymorphs are a few histiocytes ; these are larger than polymorphs, and their nuclei are round or oval and have distinct chromatin granules. The grey background is composed of fibrin.

a. Polymorph. *b*. Histiocyte.

FIG. 3.—A small vessel cut transversely is shown ; its wall is swollen and œdematous. In the lumen, in the wall and outside the wall polymorphs can be identified.

a. Polymorph.

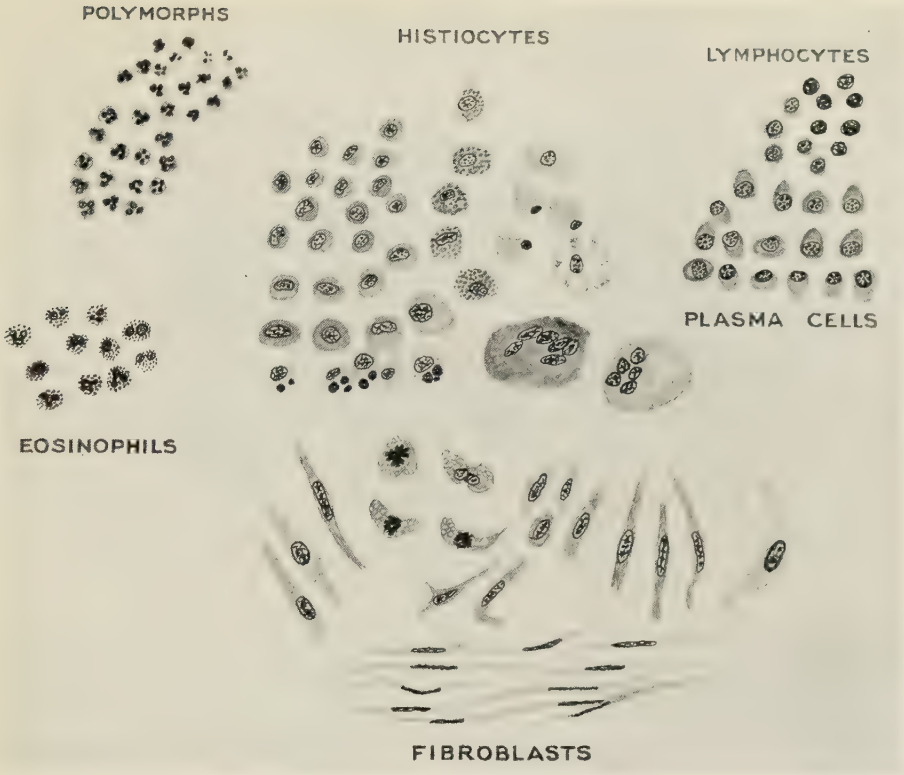
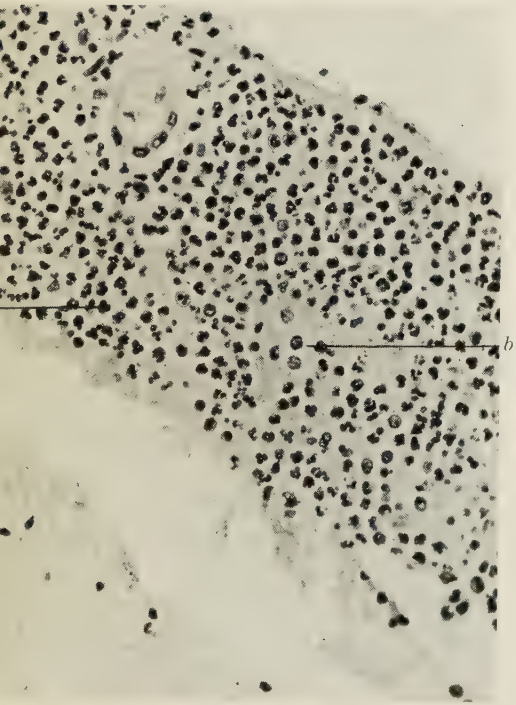


FIG. 1.



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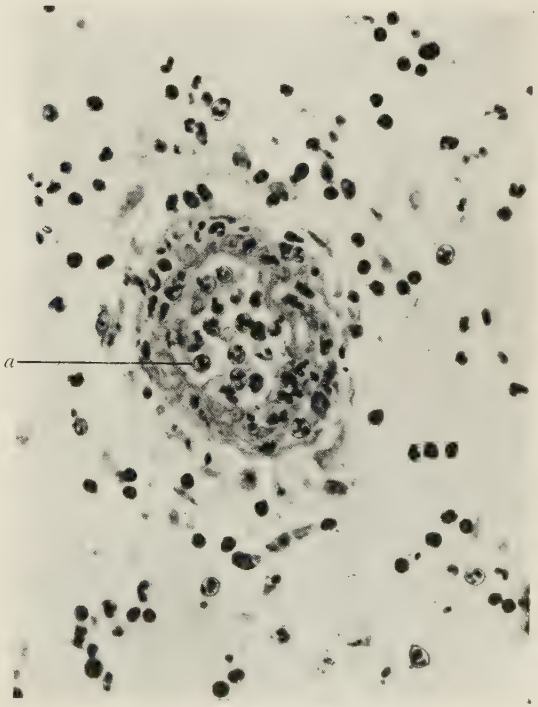

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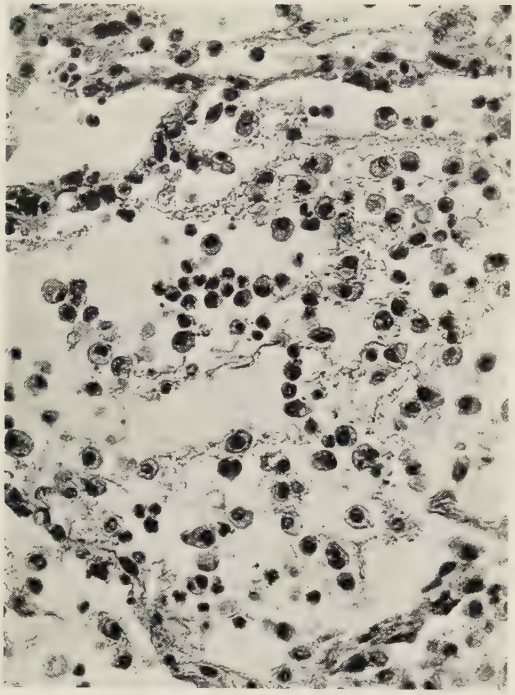

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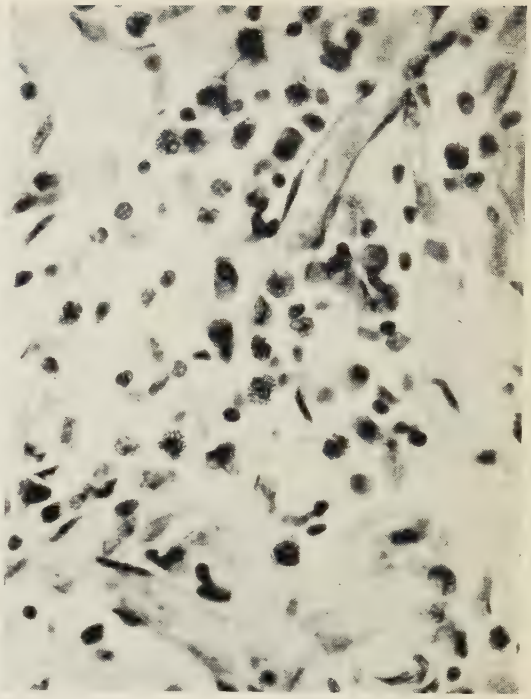

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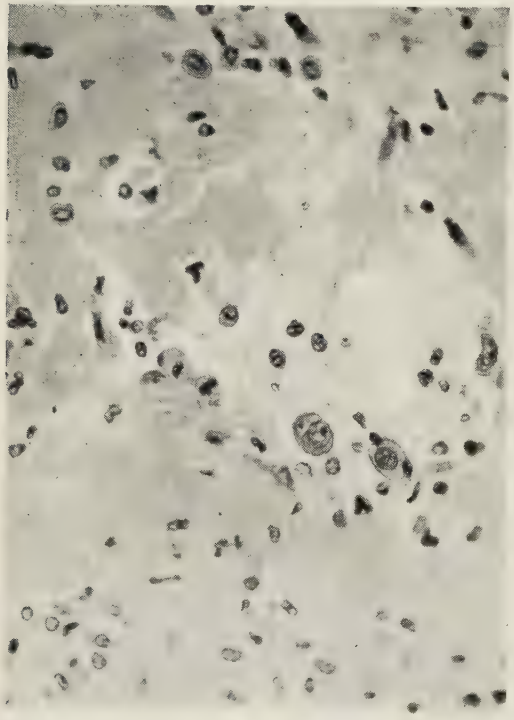

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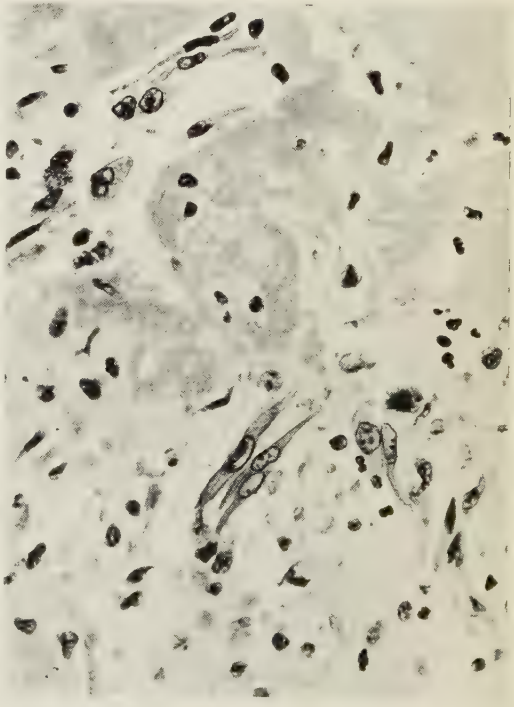


FIG. 7.

FIG. 4.—Numerous histiocytes, a few polymorphs and a delicate net of fibrin are shown in this alveolar exudate. The histiocytes are bigger than the polymorphs, have round or oval nuclei and abundant protoplasm, in which are a few minute vacuoles.

FIG. 5.—A number of eosinophil leucocytes are to be seen in this reaction.

FIG. 6.—Large histiocytes (endothelial cells), fibrin and polymorphs in an acute inflammatory exudate.

FIG. 7.—Fibroblasts growing into a fibrinous exudate : one to the right of the middle of the figure is in the process of division, and another near the top left-hand corner has just divided and the two new cells are still in contact.

Wounds and Granulation Tissue

A SECTION of a clean surgical wound shows a small amount of fibrin glueing together the cut edges of the tissues, and a slight reaction composed of leucocytes, histiocytes and fibroblasts. Such a lesion heals with the production of the minimum amount of fibrosis necessary to form a good union. The ligatures excite a reaction consisting of granulation tissue in which are numerous foreign body giant cells, and those that can be are slowly absorbed while the others become encased in giant cells or in fibrous tissue. Should a wound become infected the healing takes place by "second intention." This means that granulation tissue develops in the deepest part and spreading upwards eventually fills the gap ; the granulation tissue being in turn replaced by collagen fibres. The epithelium in each case grows across the gap provided it is not too wide.

Granulation tissue is a vascular tissue composed of numerous newly formed blood-vessels, histiocytes and fibroblasts, the whole being infiltrated with polymorphs. In addition, eosinophils, plasma cells and lymphocytes are frequently present. Eosinophils are a little larger than polymorphs, they may have a bilobed or a single round nucleus, their protoplasm contains granules which stain brightly with eosin and are frequently so numerous as to appear to have burst their cell membranes. Plasma cells are larger egg-shaped cells with abundant basophil protoplasm and round nuclei ; the chromatin of which stains deeply and is arranged in clumps round the periphery, often with a central dot giving the nucleus a clock-face or cart-wheel appearance. Lymphocytes are a little larger than red cells, they have scanty protoplasm and their nuclei stain so deeply that the arrangement of the chromatin is lost. The tissue is often œdematous, so that in section the cells appear to be somewhat loosely packed. It is not peculiar to healing wounds, but is likely to occur in any inflammation in which there is delay in resolution, and is particularly common in the floor of ulcers or in the wall of abscesses. Organisation of thrombus or of a fibrinous exudate takes place by the production of similar tissue, but it is not necessarily so vascular, nor is it usually so profusely infiltrated with polymorphs as the granulation tissue described.

As granulation tissue gets older the polymorphs become less numerous, the histiocytes more conspicuous and more stuffed with fat droplets or other remains of cells, and the fibroblasts form more dense fibrous tissue. Gradually it becomes less cellular, more fibrous, and the vessels in it become closed. Finally it is represented by dense avascular fibrous tissue.

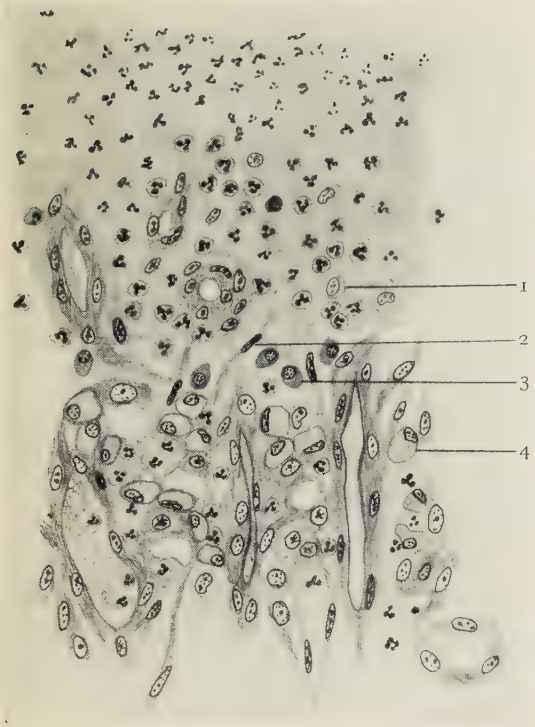
FIG. 8.—Diagram showing the floor of an ulcer : the surface consists of fibrin and degenerate cells mostly polymorphs ; deeper are capillaries, polymorphs and histiocytes, and deeper still plasma cells, fibroblasts and fat granule cells.

1. Histiocyte.
2. Fibroblast.
3. Plasma cell.
4. Fat granule cell.

FIG. 9.—Polymorphs, plasma cells, histiocytes, eosinophils, lymphocytes, fibroblasts and young capillaries are to be seen in this chronic inflammatory reaction.

FIG. 10.—Granulation tissue showing numerous young capillaries, some of which are joining up to form loops.

FIG. 11.—Granulation tissue consisting of young capillaries, plasma cells, fibroblasts, lymphocytes and polymorphs.



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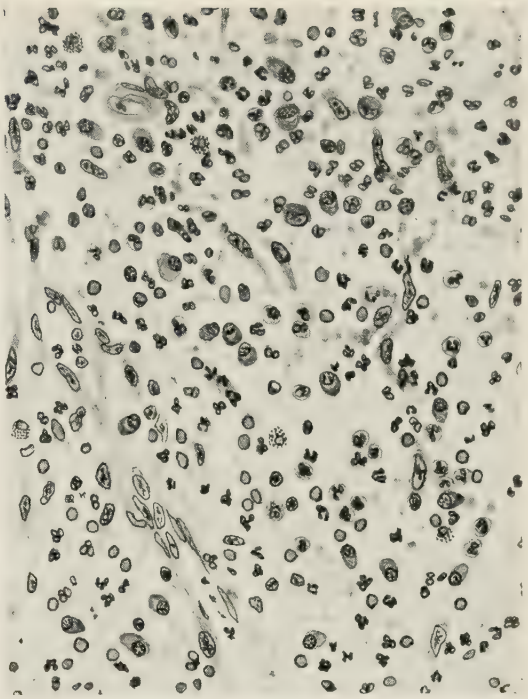
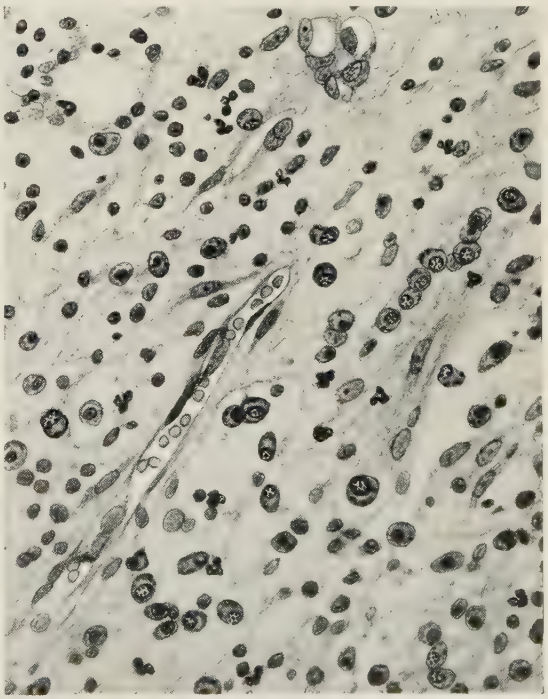


FIG. 9.

FIG. 10.



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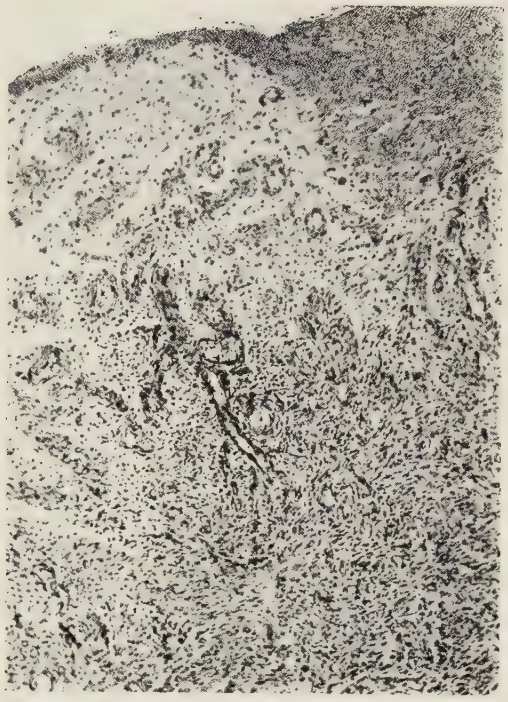

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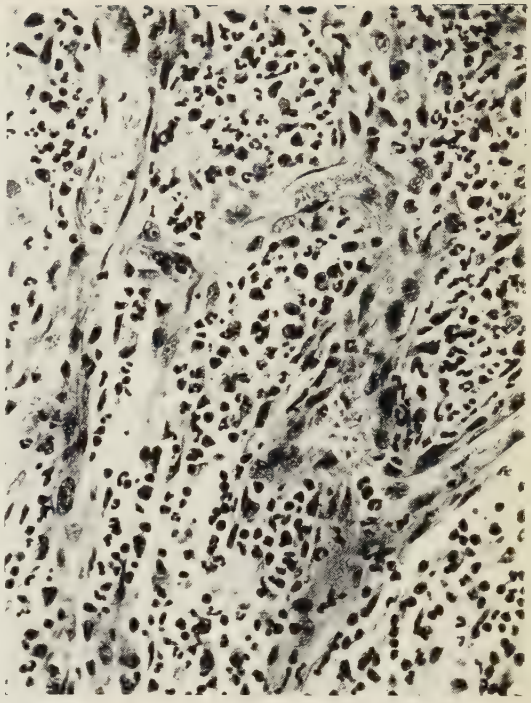
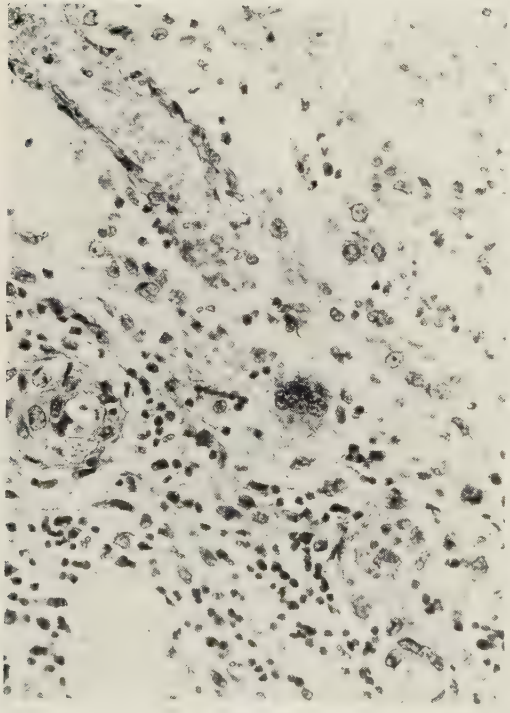


FIG. 13.



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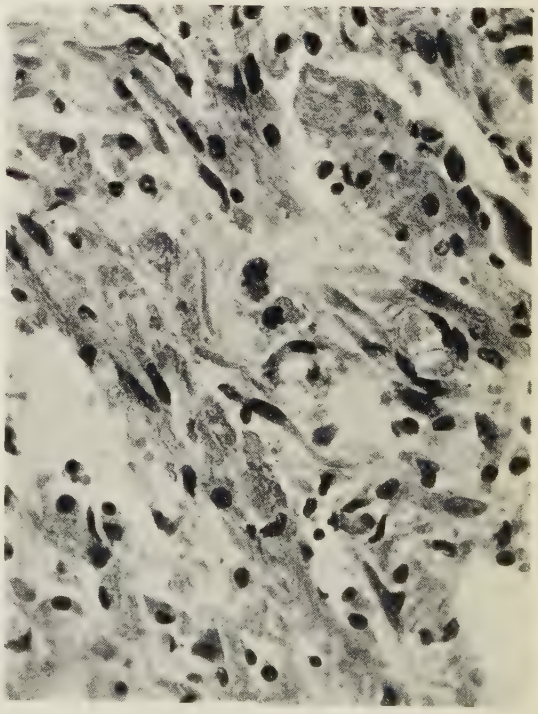


FIG. 15.

FIG. 12.—A low-power view of granulation tissue in the floor of an ulcer of skin. At the top right-hand corner is a dense patch of dead tissue (or slough) continuous with a thinner superficial layer over the rest of the surface. Beneath this the tissue is œdematous and contains numerous capillaries. In the deeper parts the tissue becomes progressively more dense.

FIG. 13.—Young capillaries forming loops in purulent granulation tissue. Swollen endothelial cells, polymorphs within and outside the lumen, plasma cells and histiocytes are to be seen.

FIG. 14.—A young capillary is shown cut longitudinally, and endothelial cells continue the line of one of its walls. Near the middle of the field is an endothelial giant cell and to the left of this is a similar mass which has developed a small lumen.

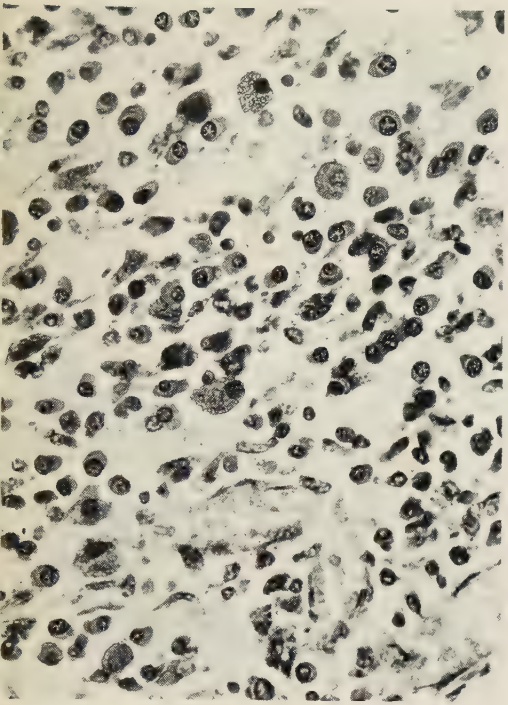
FIG. 15.—Fibroblasts with oval nuclei and long fibrous processes can be seen throughout the field. Near the middle are two fibroblasts with irregularly nodular nuclei ; these are in an early stage of mitosis. Histiocytes, and here and there a polymorph can be made out.

FIG. 16.—Part of the wall of an abscess, showing older granulation tissue in which plasma cells and fat granule cells are conspicuous.

FIG. 17.—A group of fat granule cells, also called foamy cells. They are large cells with deeply stained nuclei, and their protoplasm appears to be full of holes, the fat having been dissolved out during the preparation of the specimen.

FIG. 18.—Histiocytes in the periphery of a hæmorrhage in brain. These cells are similar to those seen in Fig. 17, except that instead of fat they have taken up blood pigment. They are called compound granular corpuscles.

FIG. 19.—A low-power view of foreign body giant cells showing their irregular outline and inspired food-stuff round which their protoplasm is wrapped. The giant cells have many oval or round well-formed nuclei, which are irregularly dispersed or grouped in them.



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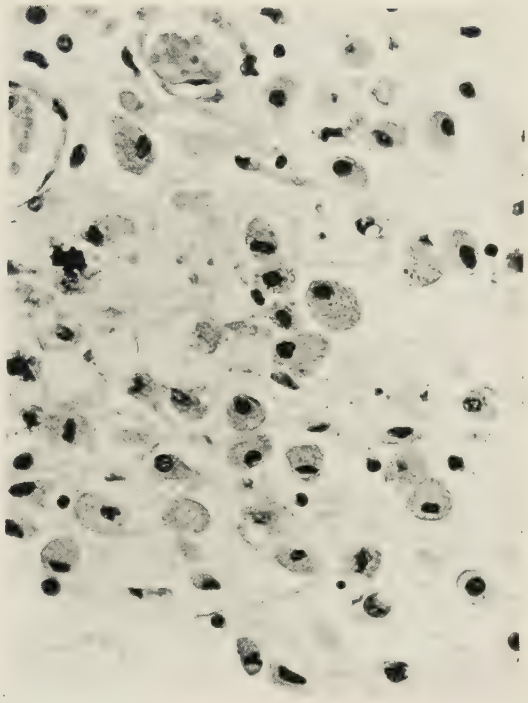

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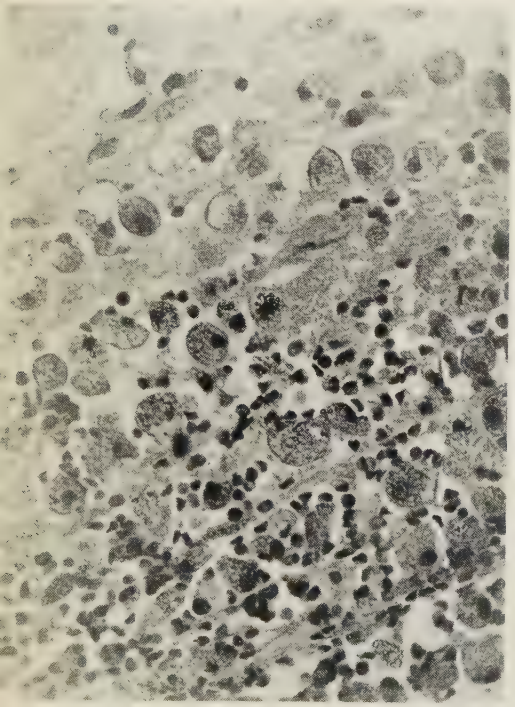

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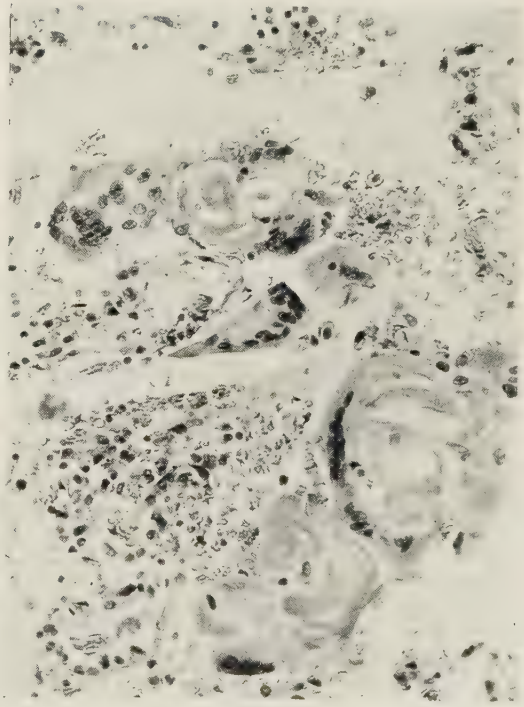

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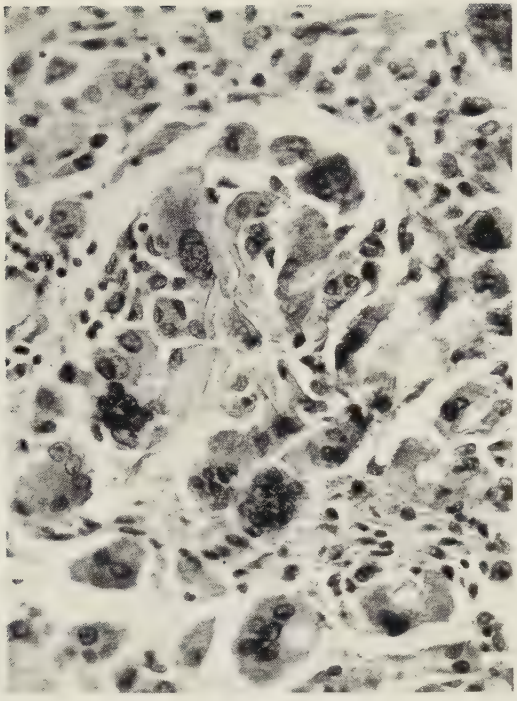


FIG. 20.

FIG. 21.

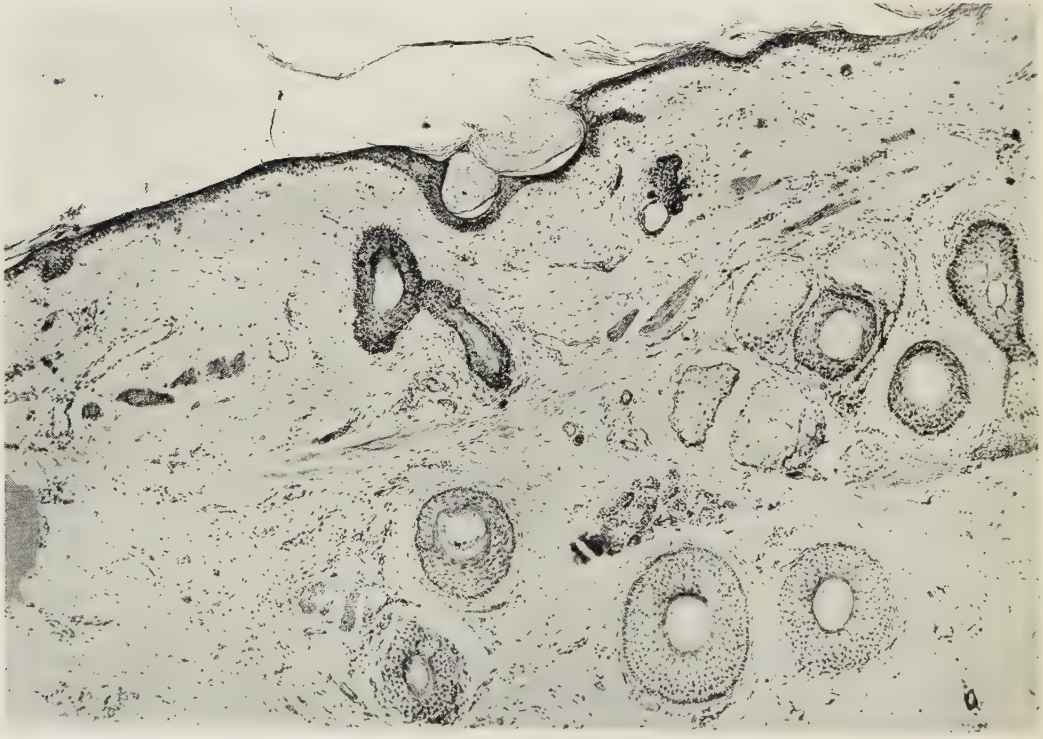


FIG. 22.

FIG. 20.—Foreign body giant cells surrounding a ligature. The fibres of the stitch have been separated, but can still be identified, and the giant cells are engulfing the majority of them. In some of the giant cells are bits of stitch which have been cut transversely and appear as vacuoles.

FIG. 21.—A scar in skin in which the dense fibrous tissue is well shown. The epithelium has formed a thin covering, and only shows slight indications of the normal papillary downgrowths.

FIG. 22.—A scar in scalp : to the right the hair follicles and sebaceous glands are numerous and conspicuous ; to the left, in the region of the scar, they are absent.

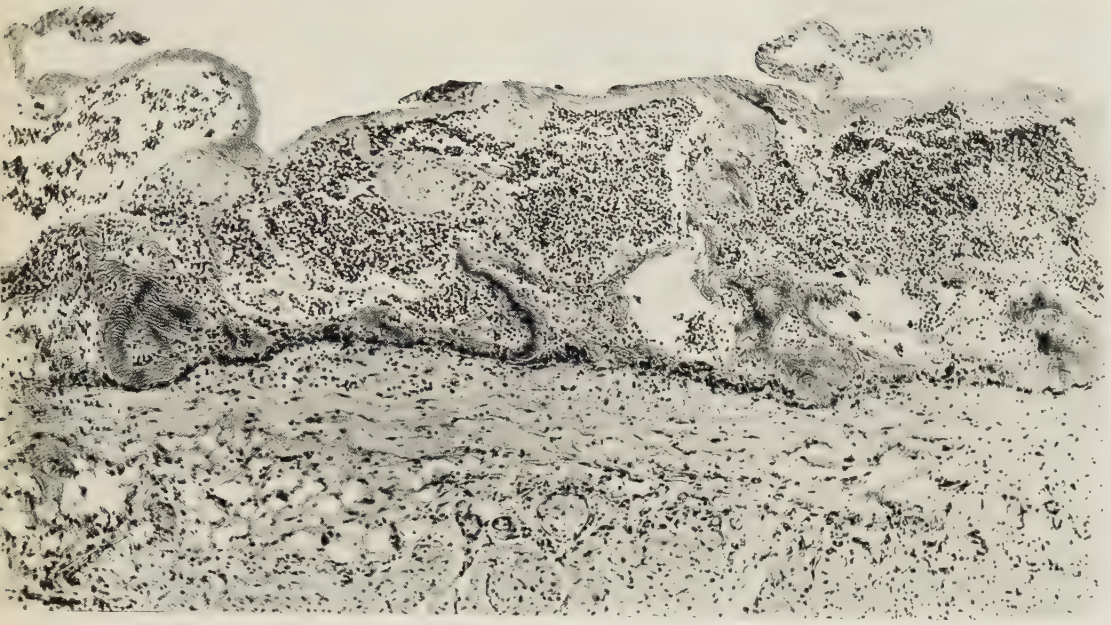
Pericarditis

INFLAMMATION of the pericardium is seen as a reaction in which lymph, polymorphs and endothelial cells form the most obvious constituents. The subpericardial vessels become distended, and from them pass plasma, polymorphs and mononuclear cells, and the endothelial cells lining the pericardium become conspicuous. Normally the endothelium which lines the pericardium consists of a single row of flattened inconspicuous cells, but when inflamed they become swollen, assume a cubical shape and proliferate. Many are cast off on the surface, and while near to their origin are easily recognised, but when they have passed out into the rest of the exudate they become indistinguishable from the histiocytes ; like them they are of irregular outline, have abundant protoplasm and well-formed round or oval nuclei. The plasma clots and forms fantastic columns and whorls connected by a net-work of less dense fibrin. In the spaces of the fibrin net and in spaces in the less solid fibrinous masses are cells the bulk of which in the acute reactions are polymorphs and histiocytes. The patient may die in the acute stage ; the exudate may resolve and the pericardium return to normal ; or organisation may take place resulting in more or less extensive fibrous adhesions between the two layers.

(Inflammations of peritoneum, pleura or other similar surfaces covered by endothelium will show changes comparable to those described for pericarditis.)

FIG. 23.—A low-power view of an acute pericarditis in which whorls and fantastic columns of fibrin, proliferated endothelial cells and collections of cells amongst the fibrin are well shown.

FIG. 24.—A diagram of a field from Fig. 23 as seen with a high power. The proliferated endothelial cells are large, of irregular shape, with conspicuous well-formed nuclei and abundant protoplasm. Not only are they to be seen on the pericardium, but similar cells are obvious amongst the groups of cells in the fibrin. Polymorphs are seen in considerable numbers, the majority of them being well formed, while others are degenerate and fluffy.



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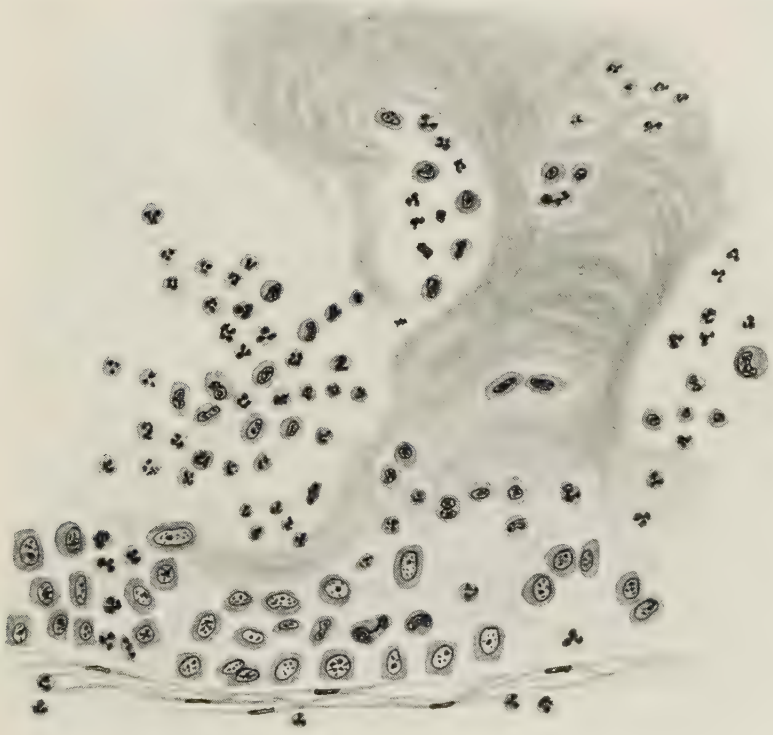


Fig. 24.

FIG. 25.

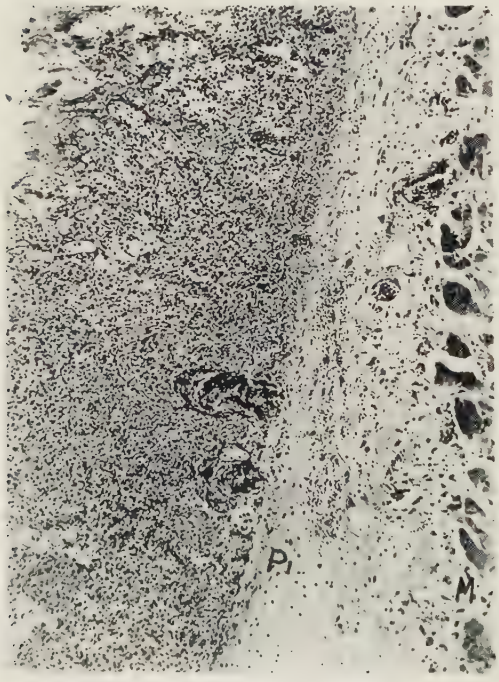


FIG. 26.

FIG. 27.

FIG. 25.—A low-power view of acute pericarditis showing the binding of the visceral to the parietal layer by fibrin. The cellular reactions and the dilated subpericardial vessels are also apparent.

M. Myocardium.
P^1. Visceral pericardium.
P^2. Parietal pericardium.

FIG. 26.—Acute pericarditis showing fibrin arranged mostly as a net.

M. Myocardium.
P^1. Visceral pericardium.

FIG. 27.—Acute pericarditis showing proliferation of endothelial cells and irregular arrangement of fibrin.

M. Myocardium.
P^1. Visceral pericardium.
E. Endocardium.

FIG. 28.—Organisation of fibrinous exudate ; the solid masses of fibrin are surrounded and in places invaded by cells. Numerous small vessels can be seen, and fibroblasts—long spindle-shaped cells—are conspicuous.

FIG. 29.—Fibroblasts growing into the exudate of a pericarditis. They have oval nuclei with well-marked outline and chromatin net. Their protoplasm is drawn out to form long tapering processes ; in some it appears to be finely reticular.

FIG. 30.—Organisation of fibrin as seen under a higher power. The dark mass is the fibrin ; this is infiltrated by small cells with dark nuclei. These are mostly polymorphs, and farther out are numerous histiocytes ; a few fibroblasts can also be identified.

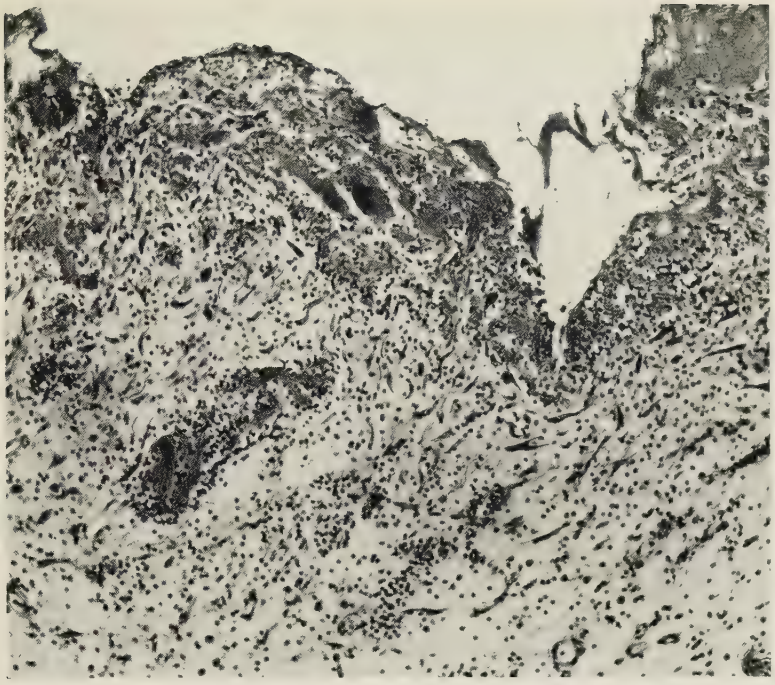


FIG. 28.

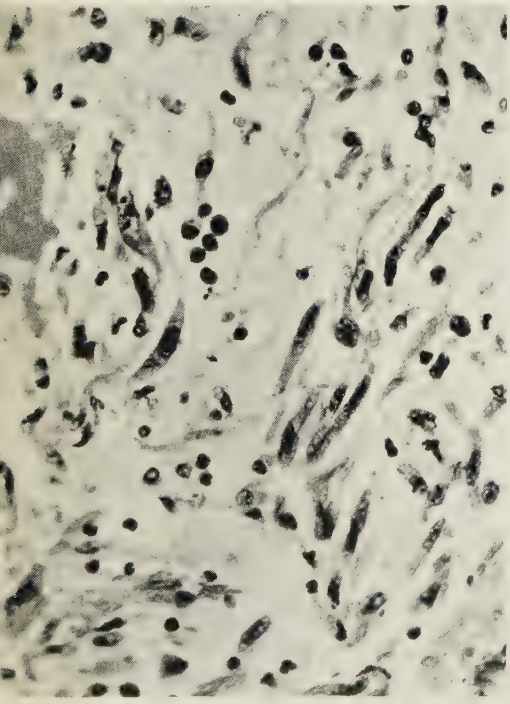


FIG. 29.

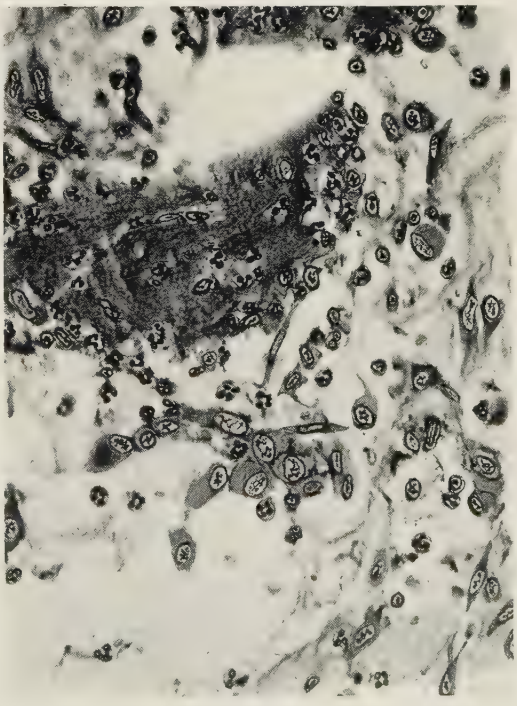


FIG. 30.

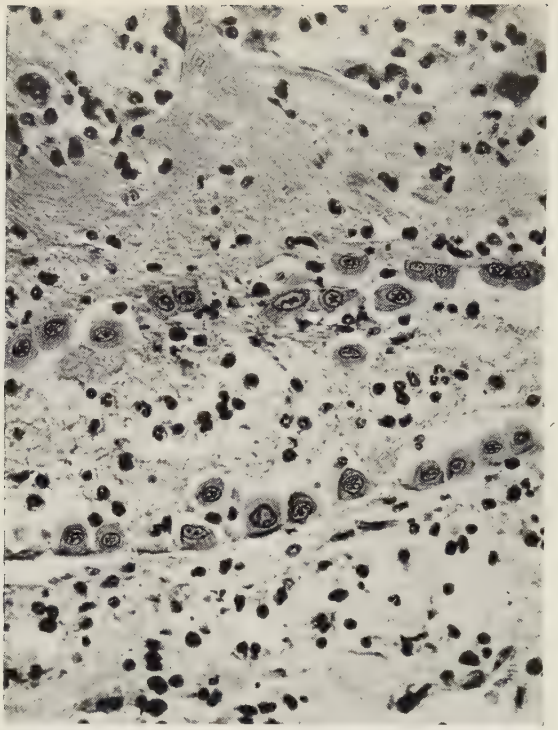


Fig. 31.

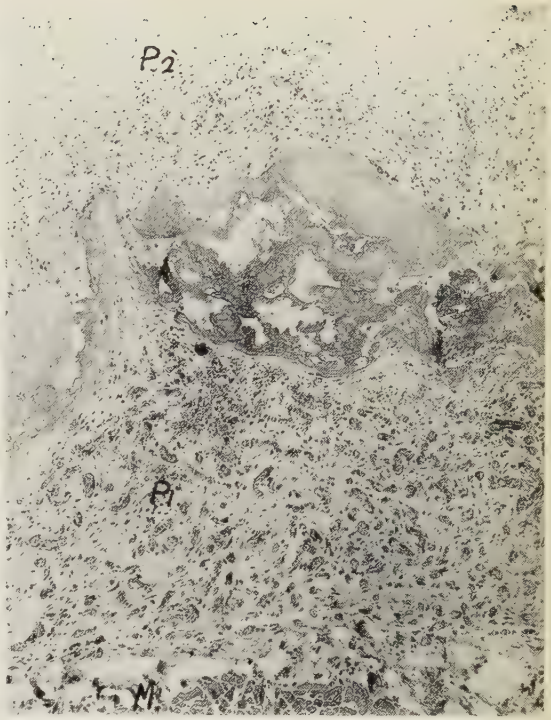


Fig. 32.

Fig. 33.

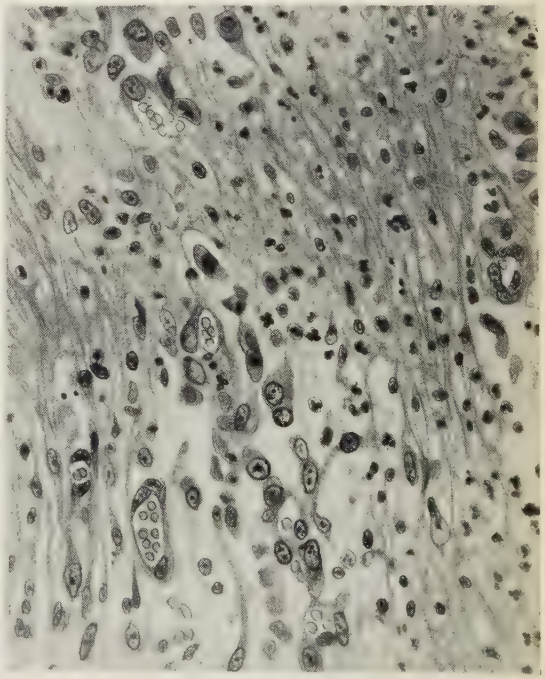


Fig. 34.

FIG. 31.—An organising exudate in which endothelial cells have formed a more or less complete lining to a space in the fibrin. The endothelial cells are similar to those shown in Fig. 24. In the space is a delicate net of fibrin, a few polymorphs and a few histiocytes.

FIG. 32.—A low-power view of organisation of exudate in which both layers of pericardium are shown. Masses of fibrin are seen between the two layers. Very numerous new vessels are present, particularly in the visceral part. A little to the left of the middle, fibrin has been replaced by young fibrous tissue joining the two layers.

M. Myocardium.
P^1. Visceral pericardium.
P^2. Parietal pericardium.

FIG. 33.—A low-power view of parietal and visceral layers of pericardium in which few dark patches of fibrin are to be seen, the two layers being bound together by young fibrous tissue. Round the fibrin are collections of phagocytes.

M. Myocardium.
P^1. Visceral pericardium.
P^2. Parietal pericardium.

FIG. 34.—A high-power view of a field in Fig. 33, showing a patch of almost completely organised fibrin surrounded and infiltrated by polymorphs and histiocytes, while in the periphery fibroblasts and new capillaries can be identified.

Abscesses

AN abscess is a localised focus of inflammation in the substance of a tissue or organ. In its acute stage it consists of a central mass of polymorphs surrounded by a more or less well-defined wall of compressed tissue and dilated vessels. The polymorphs nearest to the centre appear to be poorly formed, their protoplasm being pale, the cell outline often lost and the nuclei broken up ; degenerate polymorphs form the chief cell content of pus. Amongst these cells necrotic remains of tissue that has been replaced by the abscess may be made out, and in some cases the bacteria causing the reaction may also be present. In the periphery histiocytes and fibroblasts collect, the histiocytes frequently becoming loaded with fat droplets derived mostly from degenerate polymorphs ; and the fibroblasts arrange themselves to form a wall round the abscess. If the abscess is not quickly resolved the histiocytes and fibroblasts increase in number and new blood-vessels are formed. In this way a very vascular wall composed of young fibrous tissue, histiocytes, polymorphs and numerous new vessels is produced, and is called granulation tissue.

The abscess may burst, the pus escaping from the surface and the granulation tissue becoming replaced by fibrous tissue : the granulation tissue may spread in from the circumference and replace the pus and in turn be replaced by fibrous tissue, or the pus may become dried up and the granulation tissue become more and more dense until it forms a fibrous wall round a central necrotic mass.

FIG. 35.—Acute abscess in submucosa of small intestine : some of the central part has fallen out ; the irregular black dots near the middle are groups of cocci ; the compressed tissue, forming a thin wall, can be seen.

FIG. 36.—Acute abscess in myocardium : this abscess is similar to the one in Fig. 35, save that the wall is not so clear and the clumps of cocci are in the upper and right-hand corner of the abscess.

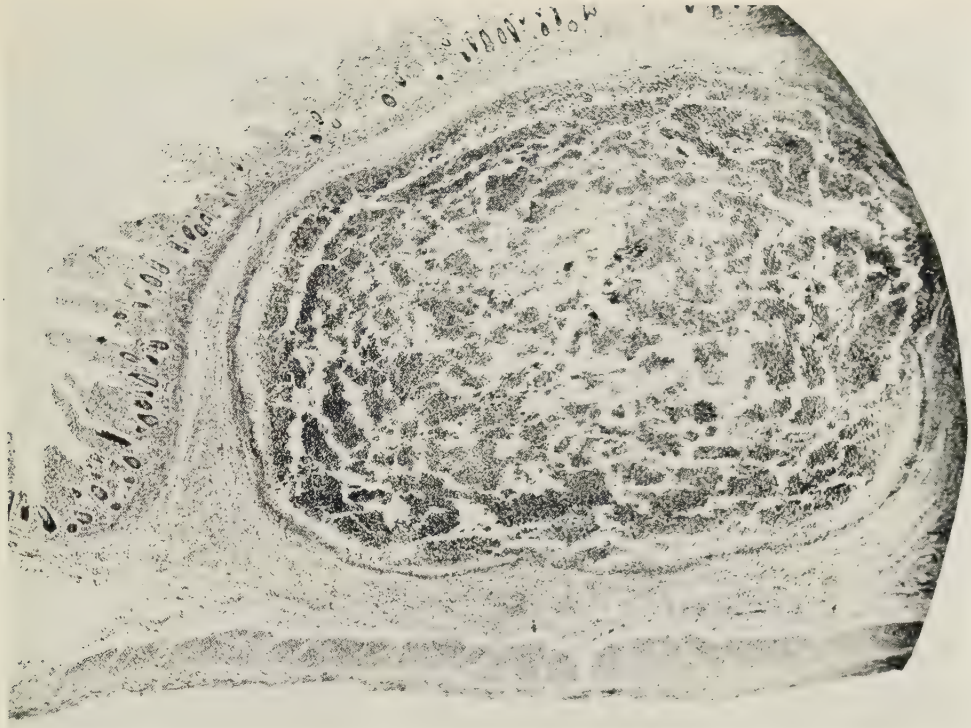


FIG. 35.

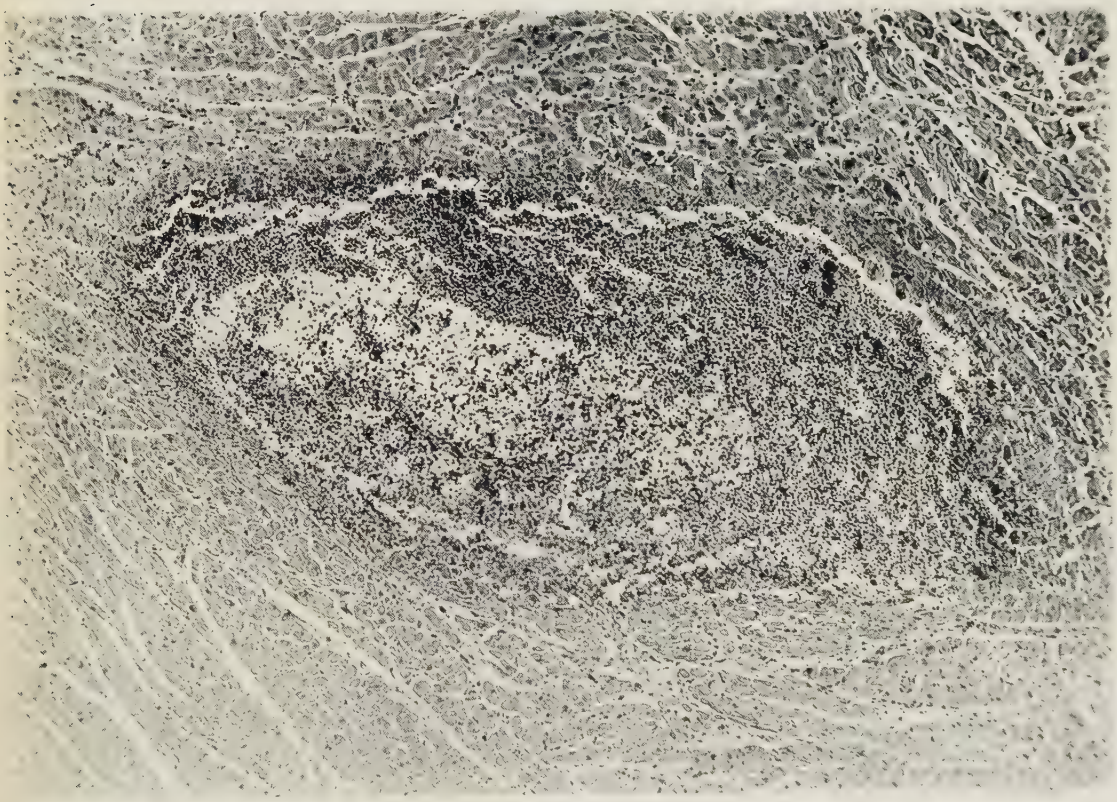


FIG. 36.

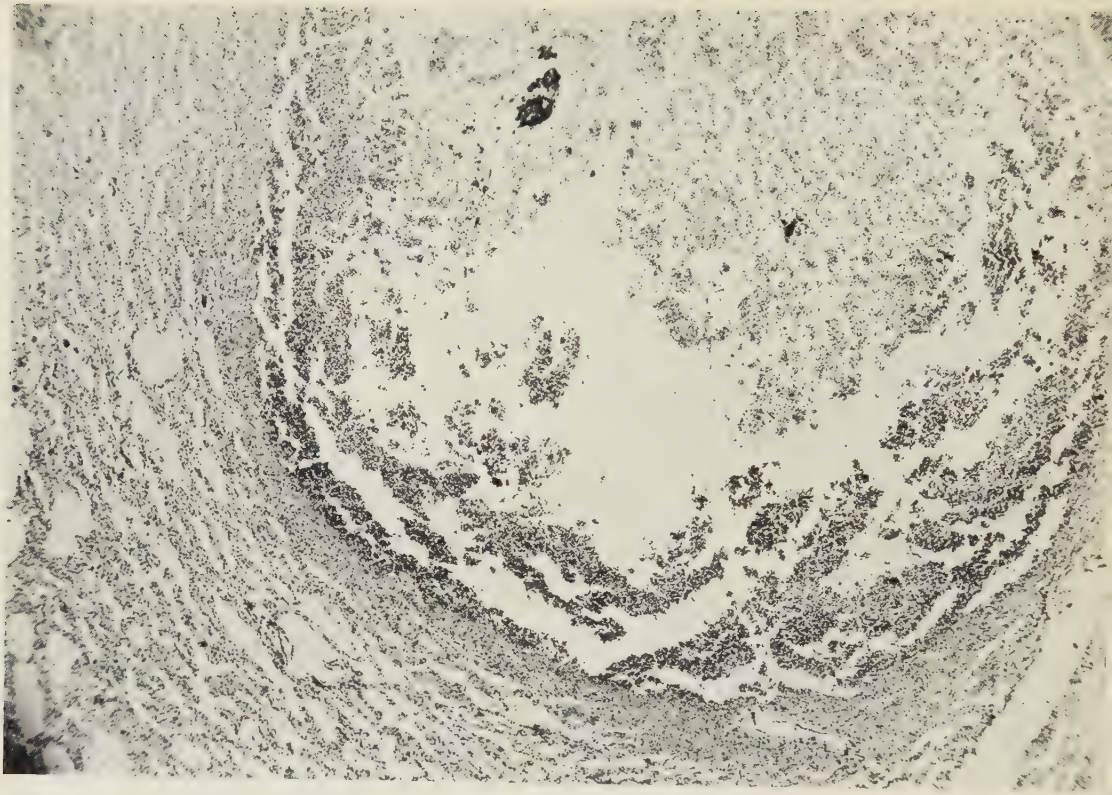


Fig. 37.

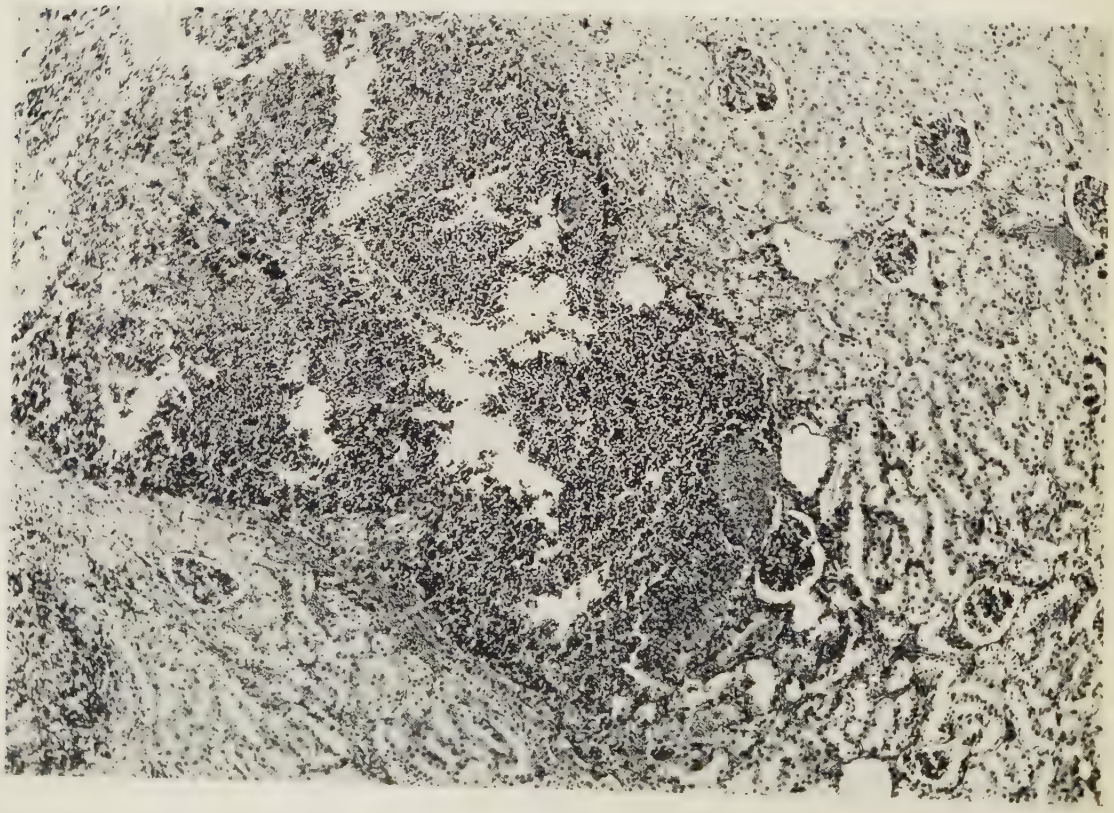


Fig. 38.

FIG. 37.—Acute abscess in lung: more of the pus has escaped in this section than in the two previous ones; the compressed lung tissue forming a wall, and the black dots representing clumps of cocci are well shown.

FIG. 38.—Acute abscess in kidney: the compressed partly necrotic tissue of the kidney forming a wall to the abscess is best seen around its lower and right-hand borders; some of the exudate has escaped, and the clumps of cocci are surrounded by polymorphs in the left part of the abscess.

FIG. 39.—Acute abscess in liver : the general appearance of the abscess is similar to the former examples ; the compressed liver tissue and the fairly wide zone of necrosed liver tissue on the right are well shown.

FIG. 40.—Periphery of abscess in myocardium : some of the muscle bundles stain more deeply and have lost their striations, others are broken up ; the muscle nuclei are degenerate, some being stained deeply while others are fragmented. Polymorphs are infiltrating the degenerate bundles. (The normal pigment granules near the nuclei in some of the muscle bundles can be seen.)

FIG. 41.—Periphery of abscess in liver, showing degenerate compressed liver cells and degenerate polymorphs.

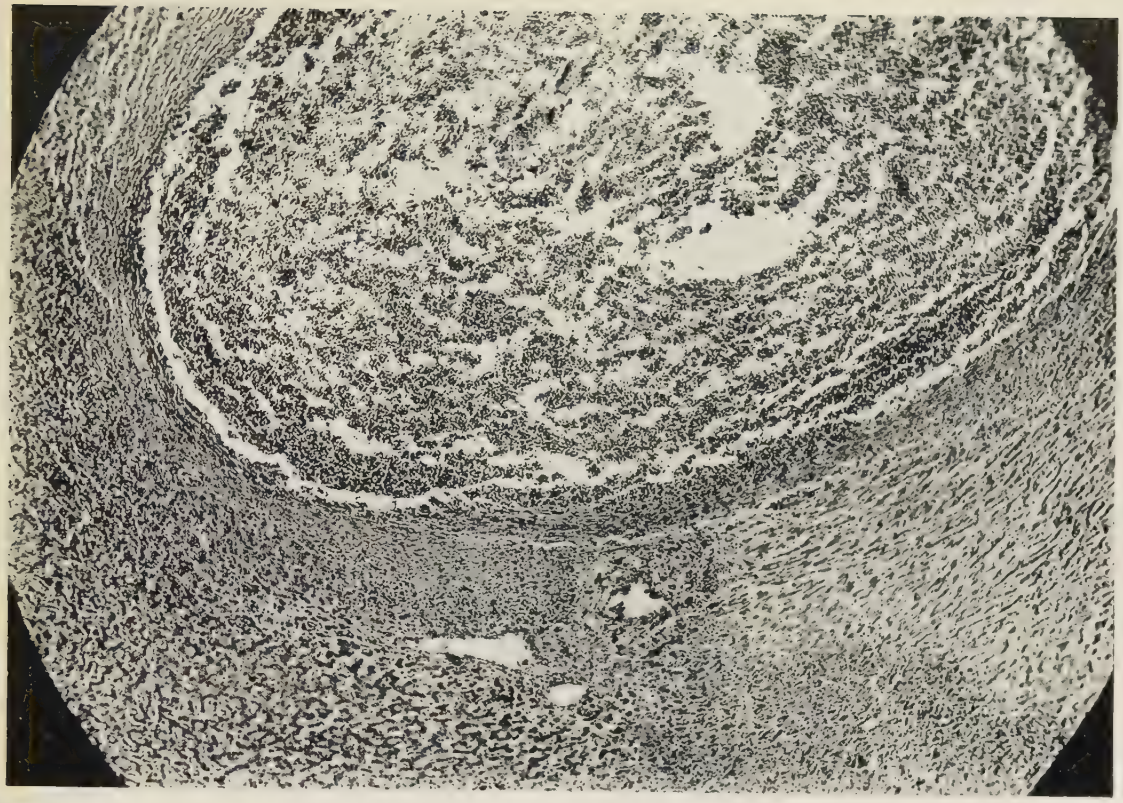


FIG. 39.

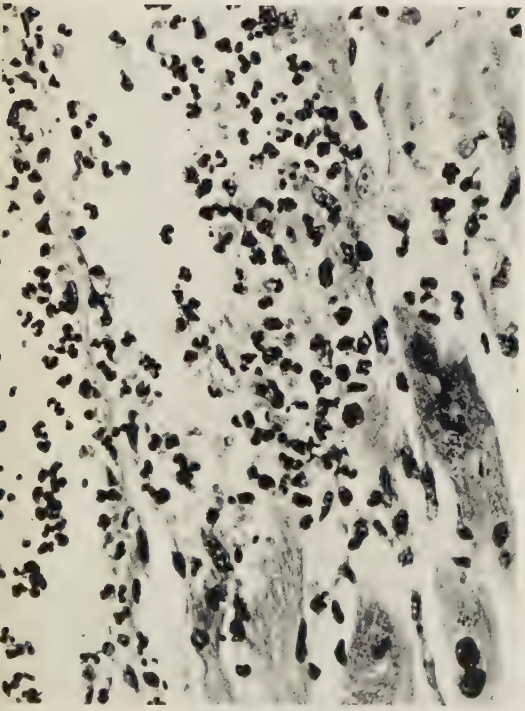


FIG. 40.

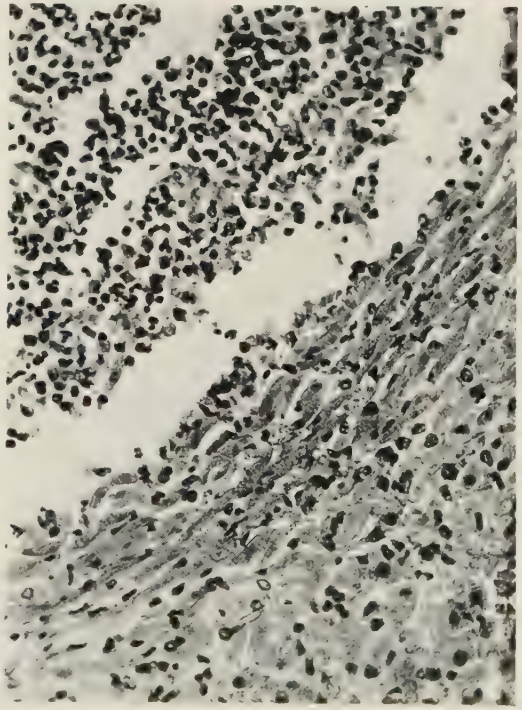


FIG. 41.

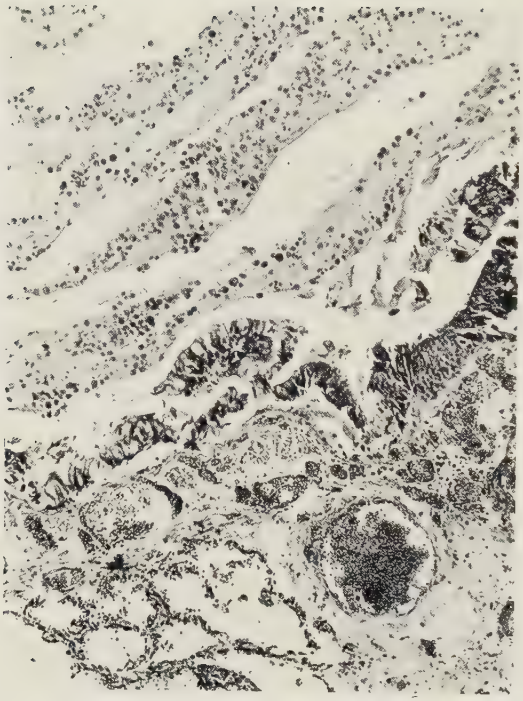


FIG. 42.

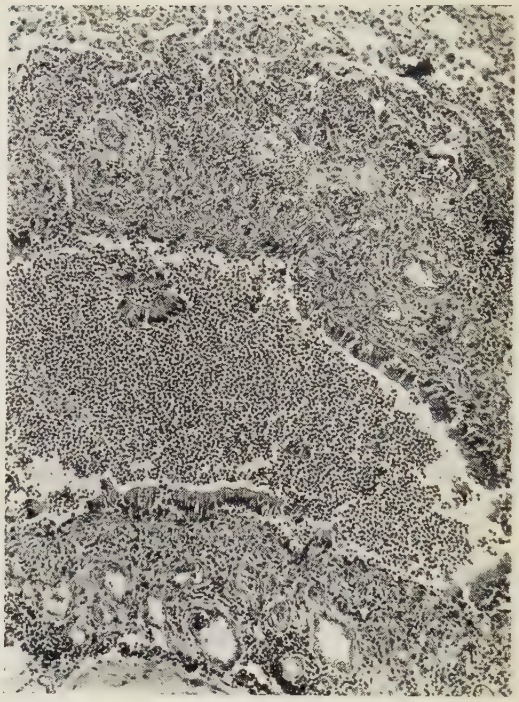


FIG. 43.

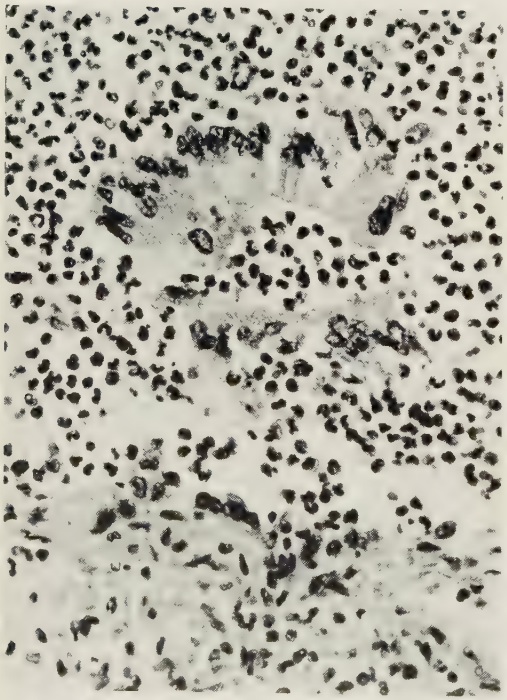


FIG. 44.

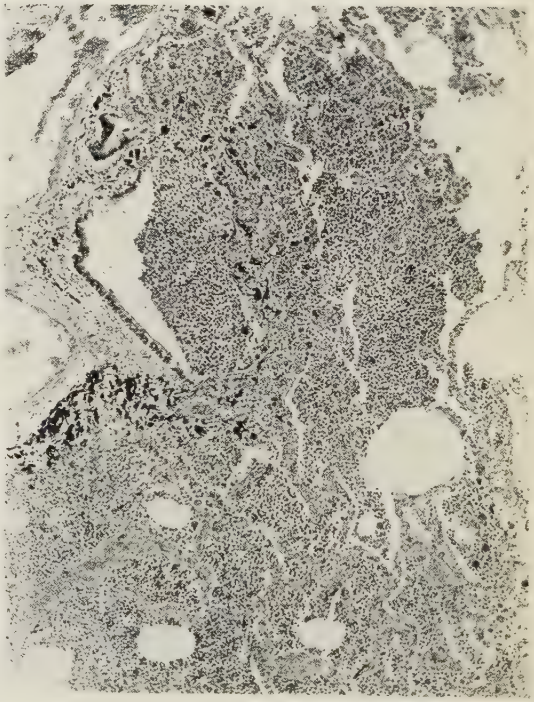


FIG. 45.

Bronchitis and Broncho-pneumonia

INFLAMMATION of a surface covered by columnar mucus-secreting cells commonly begins with an outpouring of mucoid fluid and desquamation of epithelial cells ; this is called a catarrhal inflammation. An early stage of acute bronchitis forms an excellent example of this type of reaction. In it the mucous membrane becomes swollen, the vessels in the submucosa engorged and the lumen filled with mucus ; epithelial cells become detached individually or in small groups, and if the reaction continues polymorphs permeate the wall and reach the lumen. With the advent of the polymorphs in the lumen the term muco-purulent is applied, and if they become still more numerous and the mucus less evident the reaction is called purulent.

Should the inflammatory reaction spread beyond the bronchi or bronchioles to the surrounding alveoli a nodular or lobular consolidation of the lung results called broncho-pneumonia. The essential difference between broncho-pneumonia and lobar pneumonia is that in the former the inflammation starts in the bronchi and bronchioles and spreads to the alveoli. The characteristic histological picture of broncho-pneumonia is pus in a bronchiole continuous with pus in alveoli ; and an exudate, in one field of which the alveoli may be full of polymorphs, in another of histiocytes and in another of œdema.

FIG. 42.—Mucous bronchitis showing mucus and polymorphs in the lumen, slight desquamation of columnar cells and congestion of the wall of a bronchus.

FIG. 43.—Purulent bronchitis showing a mass of polymorphs filling the lumen, desquamation of columnar epithelium and spread of the inflammation to the wall and alveoli in the neighbourhood of the bronchus.

FIG. 44.—A high-power view of the desquamated columnar cells and the polymorphs shown in Fig. 43.

FIG. 45.—Broncho-pneumonia showing pus in a bronchiole and in the alveoli around it. (The soot granules in the peribronchial tissue are well shown.)

FIG. 46.—A low-power view of broncho-pneumonia showing the uneven consolidation, pus in a bronchiole and neighbouring alveoli, histiocytes in alveoli and other alveoli full of clotted fluid.

FIG. 47.—A high-power view of a field taken from Fig. 46, showing the plasma and histiocytes.

FIG. 48.—Another high-power view showing an alveolus filled with polymorphs and histiocytes and its neighbour containing histiocytes and very few polymorphs.

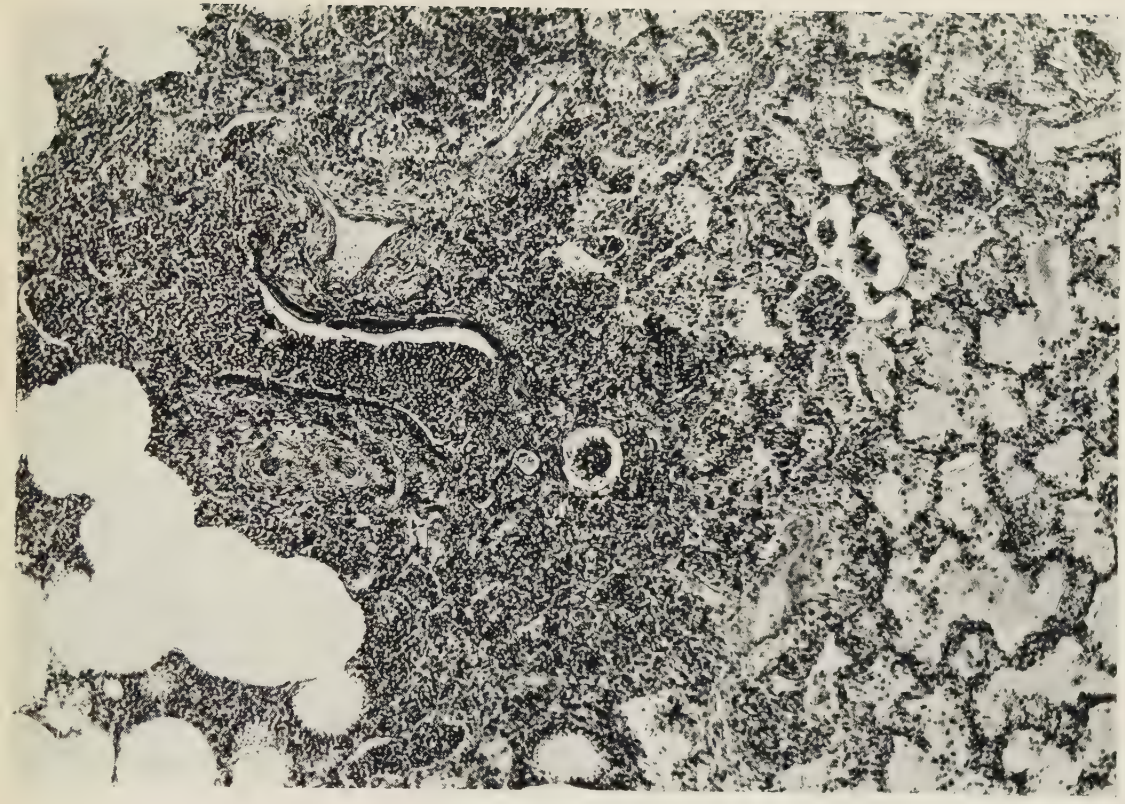


FIG. 46.

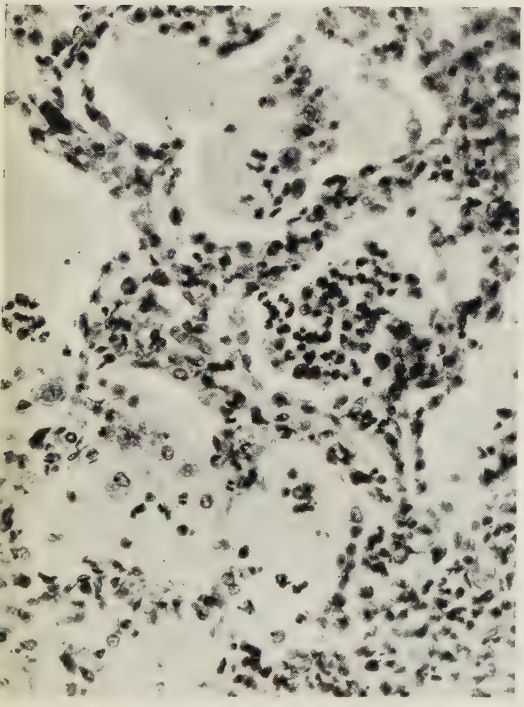


FIG. 47.

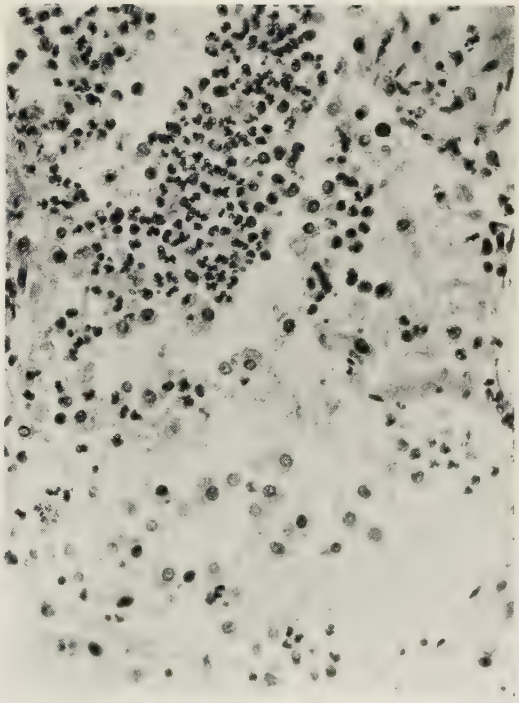


FIG. 48.

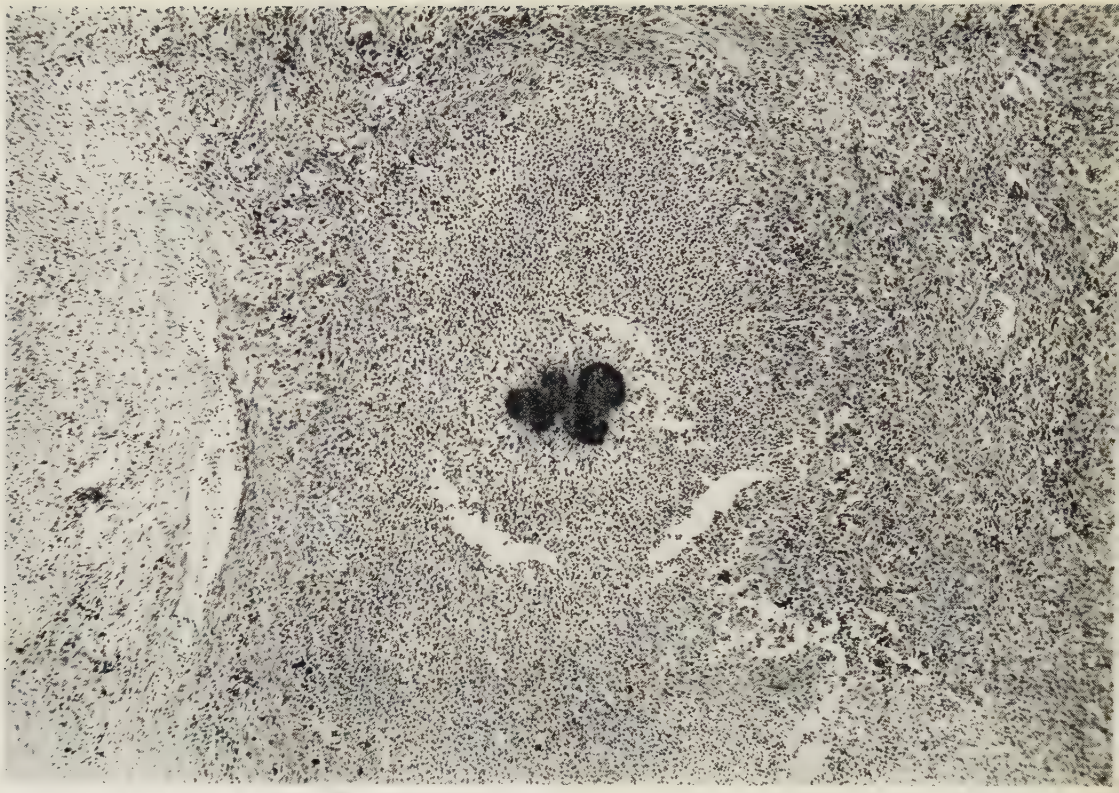


FIG. 49.

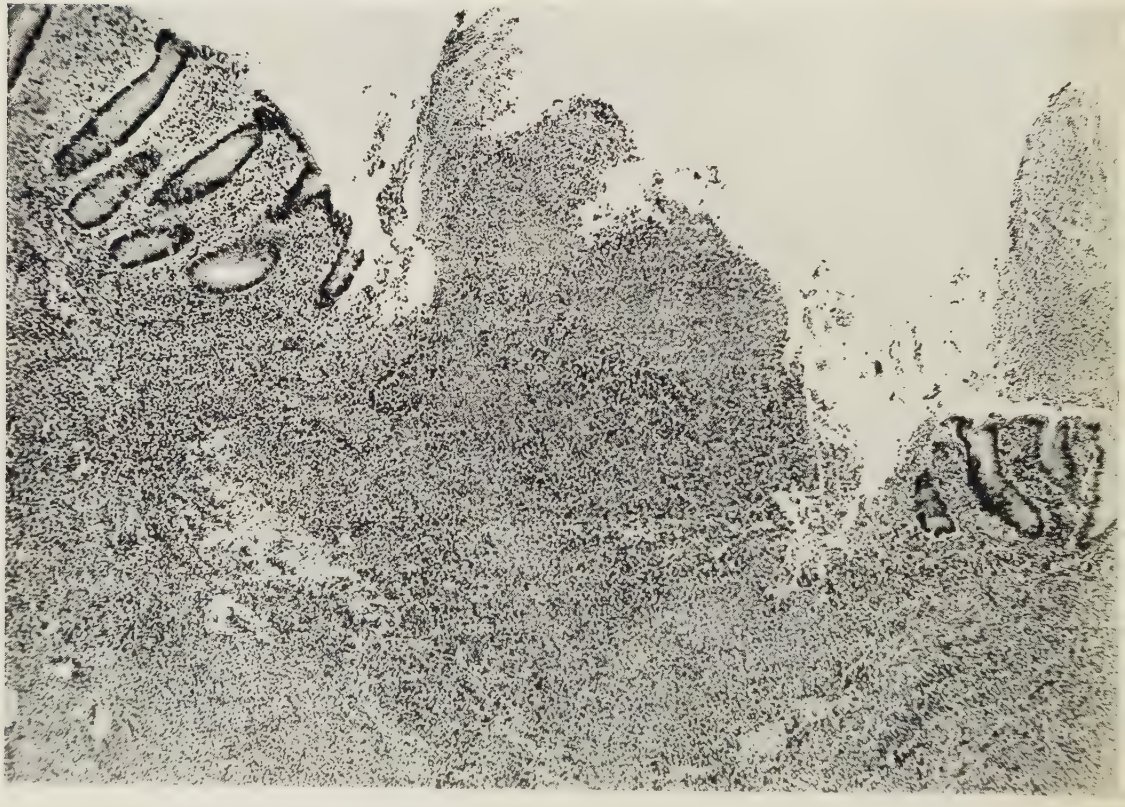


FIG. 50.

Actinomycosis

THIS is a chronic purulent inflammation fairly common in cattle and less common in man. It is characterised by progressive abscess formation in organs, or ulceration of a surface. The abscesses are made up of a central pool of pus, in which a colony of the *Streptothrix actinomyces* is often conspicuous, surrounded by granulation and fibrous tissue. They spread by burrowing through the tissues, forming groups of abscesses the walls of which are in contact; in this way a honeycomb-like net-work of fibrous and granulation tissue is produced, each space being filled with pus and mycelium.

FIG. 49.—Actinomycotic abscess showing the mass of streptothrix with radiating clubs in a central position surrounded by a wide zone of polymorphs, and farther out a fairly dense granulation and fibrous tissue.

Appendicitis

INFLAMMATION of the appendix occurs commonly and in all degrees of severity, the histological appearances being similar to that of a reaction of equal intensity in any other organ. The example illustrated here is a severe one in which polymorphs have infiltrated the mucosa, submucosa, muscularis and serosa. An inflammation spread diffusely throughout an organ in this way is often called a phlegmon or a phlegmonous inflammation.

FIG. 50.—Acute appendicitis showing pus bursting through the mucous membrane of the appendix and infiltrating the submucosa.

Diphtheria

THE local lesions produced by the diphtheria bacillus consist of necrosis of tissue and the formation of a membrane, which is most commonly formed on the fauces, tonsils, pharynx or larynx, and rarely spreads down the trachea or œsophagus. The membrane consists of a dense felt-work of fibrin, containing patches of necrosed mucosa, and numerous leucocytes. Where the necrosis is intense the membrane is attached firmly to the underlying tissue by fibrin, elsewhere it overlaps, but is easily separated from the mucosa. The inflammation extends for some distance into the submucous connective tissues, which become congested, œdematous and infiltrated with polymorphs.

FIG. 51.—Diphtheria : the squamous epithelium of the fauces becomes progressively thinner from left to right, and overlapping it is a membrane of fibrin and cells which, where the epithelium is deficient, has infiltrated the subepithelial connective tissue.

FIG. 52.—Diphtheritic membrane covering a tonsillar crypt showing the absence of epithelium and the continuation of the fibrin net into the subepithelial connective tissue.

FIG. 53.—A higher power view showing the dense fibrin net and the degenerate cells, of which a diphtheritic membrane is composed.

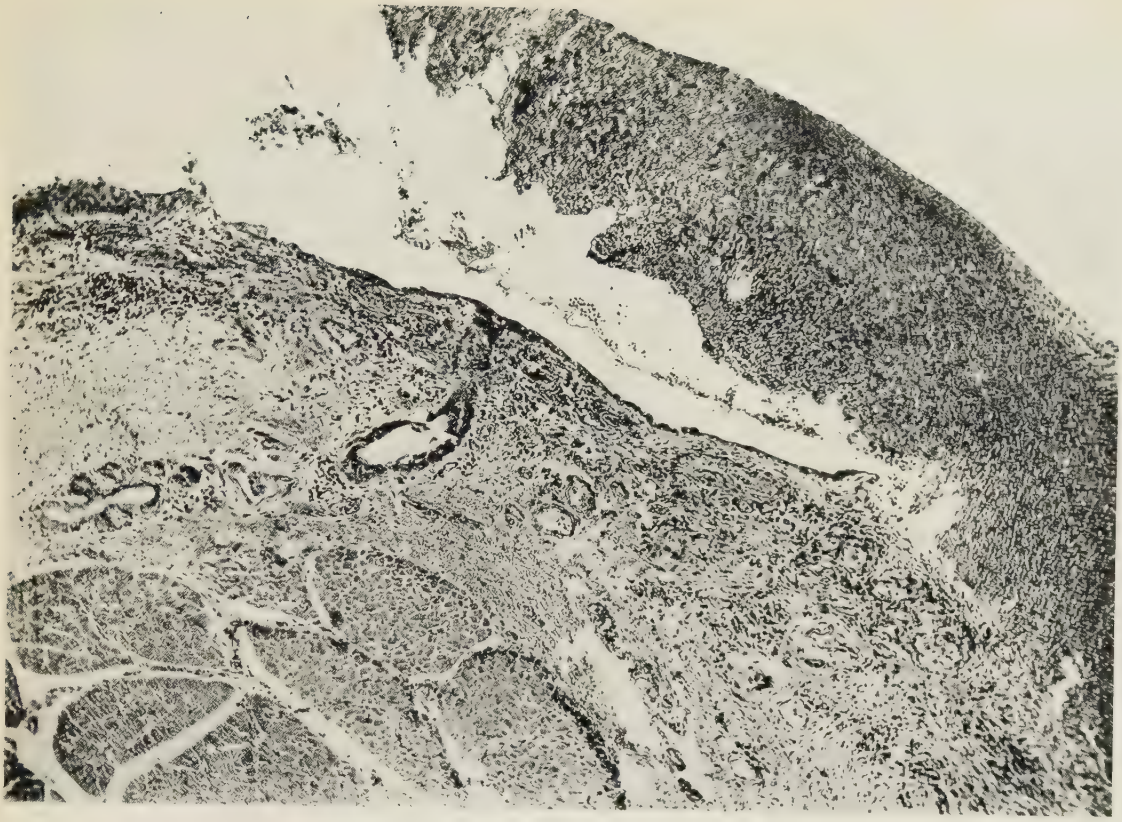


FIG. 51.

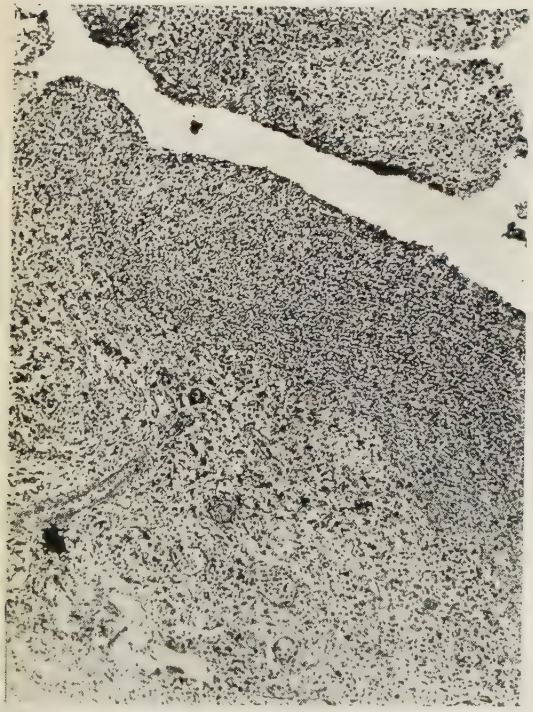


FIG. 52

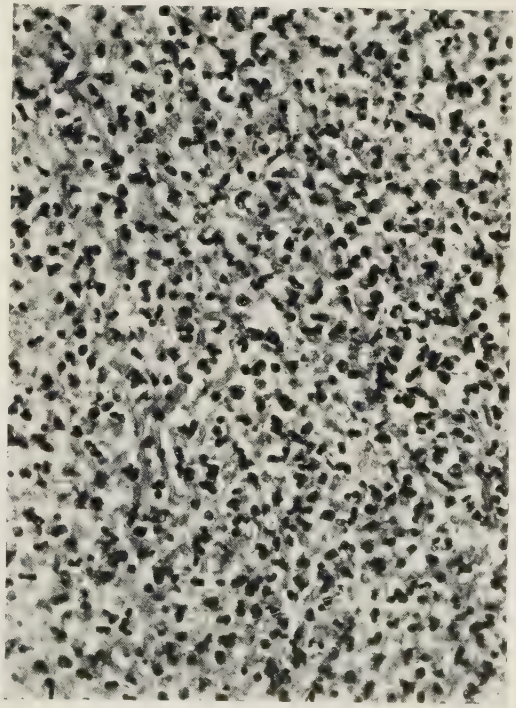


FIG. 53.

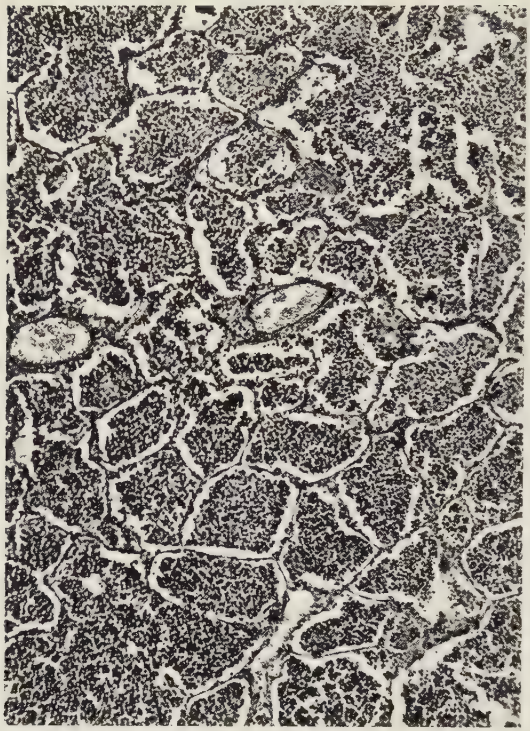


FIG. 54.

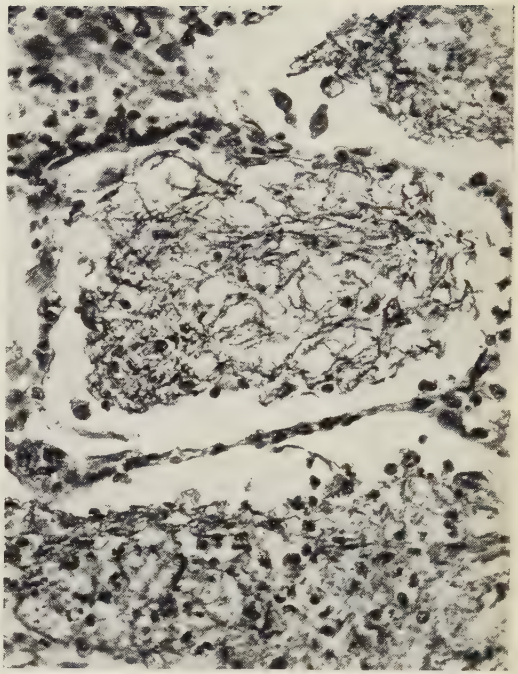


FIG. 55.

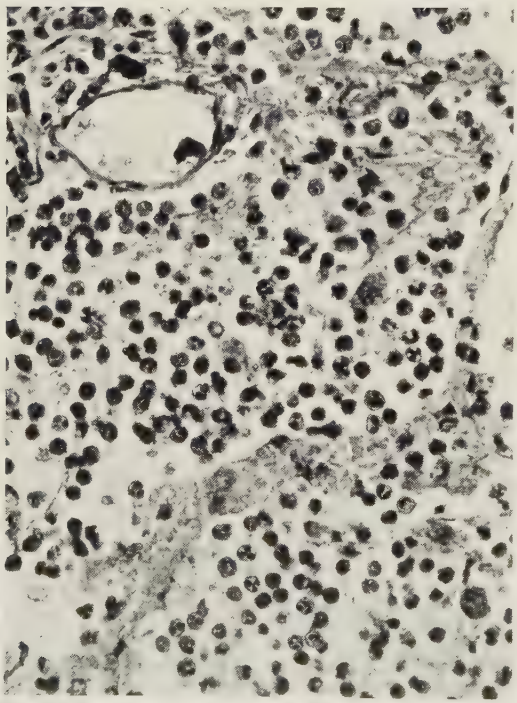


FIG. 56.

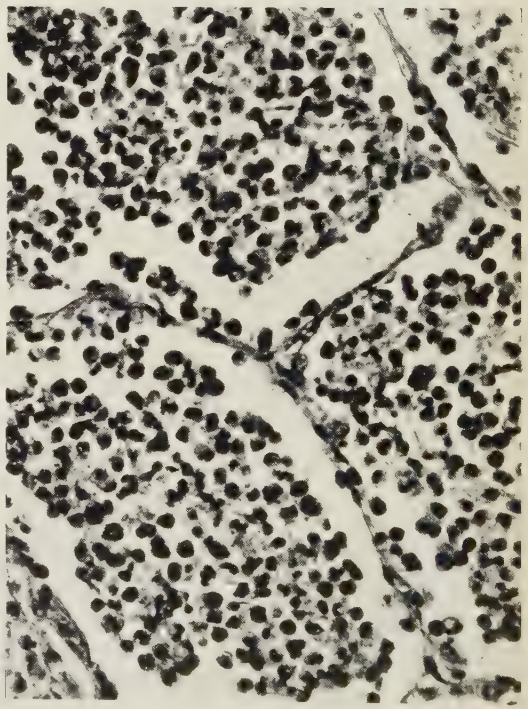


FIG. 57.

Lobar Pneumonia

THIS is an inflammation of the lung which starts in the alveoli and spreads from alveolus to alveolus, changes in the bronchi and bronchioles being of secondary importance. The exudate is not confined within any anatomical units of the lung, it may fill a whole lobe, more than one lobe, or only a part of a lobe. In the latter case it has a clearly defined edge which passes straight across the lung and does not mark out or bear any relation to the anatomical distribution of the alveoli. Although the alveolar walls remain intact they do not appear to form a barrier to the spread of the inflammation.

It is usual to describe stages in pneumonia, but it should be clearly understood that the stages are characteristic of any acute inflammation and fade one into another, and often two of them will be found in the same lung. The stages are congestion and engorgement, red hepatisation, grey hepatisation and resolution. The first is largely conjectural ; in it the capillaries forming the alveolar walls are distended with blood, and from them fluid passes into the alveoli ; except possibly at the edge of a patch of consolidation it is never seen. The next stage is the one in which in addition to the engorgement red cells have escaped into the alveoli, the exudate has become coagulated forming fibrin, leucocytes have migrated from the vessels, and cells lining the alveoli have proliferated. At this stage a section shows alveoli filled with a net-work of fibrin, in the meshes of which are well-preserved red cells, leucocytes and numerous histiocytes, and engorgement of the capillaries in the alveolar walls. As the inflammation progresses the leucocytes become more numerous, until the alveoli are so distended with them that the capillaries are compressed and appear to be closed. This is the stage of grey hepatisation, and a section now shows alveoli filled with fibrin and leucocytes. The leucocytes are mostly degenerate, and among them are a few histiocytes but no red cells, and the capillaries are inconspicuous. A combination of this and the preceding stage is the most usual post-mortem finding. Resolution consists of a liquefaction of the fibrin and to a large extent of the cellular exudate and a reopening of the capillaries ; this stage is seldom seen.

The larger bronchi usually show a mild degree of inflammation, the smaller ones and the bronchioles contain fibrinous casts. There is always an inflammation of the pleura over the consolidated part of the lung.

FIG. 54.—A general low-power view of lobar pneumonia. Apart from the slight shrinkage of the exudate, due to fixation, the alveoli are uniformly filled with cells and fibrin.

FIG. 55.—A section stained to show the fibrin net in alveoli in lobar pneumonia.

FIG. 56.—A high-power view of an exudate in a stage when the capillaries are still engorged. The fibrin net, histiocytes and polymorphs are all well seen.

FIG. 57.—A high-power view taken from a stage when the capillaries are inconspicuous. The fibrin, histiocytes and polymorphs are well shown ; many of the latter are degenerate.

Typhoid

THE local reactions in this disease occur with remarkable constancy in lymphadenoid tissue of intestine, mesenteric glands and spleen. It is usual to describe stages in the intestinal lesions, and these correspond with weeks in the progress of the disease. The first is that of swelling or medullary infiltration of the lymphatic nodules, including Peyer's patches. This is due in part to hyperæmia and œdema, but chiefly to a proliferation of histiocytes. These cells form the most characteristic feature of the reaction ; they are large, have pale-pink protoplasm and round or oval vesicular nuclei. They are actively phagocytic, and frequently contain one or more lymphocytes or fragments of other cells. The next stage is one of necrosis or slough formation. In it foci of coagulation appear which, becoming confluent, may spread through the whole swollen patch and commonly extend as deep as the inner muscle coat. The separation of the slough forms the next stage and healing the final stage. The healing is exceptionally complete, absence of muscularis mucosæ and rather smaller glands forming the mucosa usually being the only evidence of previous ulceration. The changes in lymphatic glands and spleen are similar to those described in Peyer's patches, except that necrosis in them is less conspicuous.

FIG. 58.—A diagram of a low-power view showing a swollen Peyer's patch in the early stage of typhoid.

FIG. 59.—A diagram of a low-power view at a later stage, when the greater part of a swollen patch has become necrotic and has begun to separate.

FIG. 60.—A high-power view showing the cells found in a swollen patch and in the periphery of a slough. They are histiocytes having round or oval nuclei and abundant pink protoplasm. In the protoplasm lymphocytes and fragments of other cells are often found. These cells are sometimes called typhoid cells.

FIG. 61.—Another group of histiocytes, similar to those shown in Fig. 60, from the edge of a typhoid ulcer.

Fig. 58.

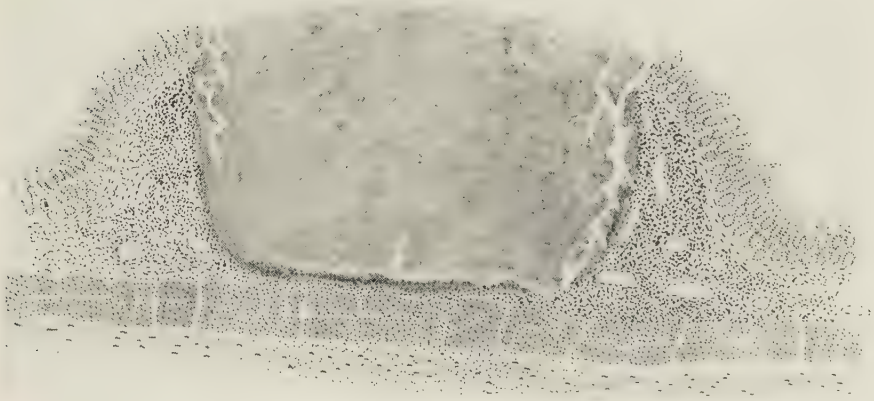


Fig. 59.

Fig. 60.

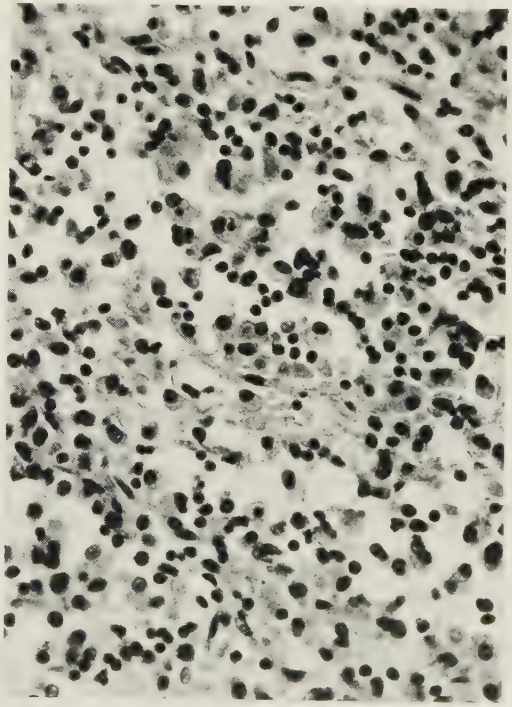


Fig. 61.

Tuberculosis

THIS is one of the granulomatous inflammations, that is, one in which the reaction of the extra-vascular tissues dominates the histological picture. The characteristic lesion of tuberculosis and the one that gives it its name is the tubercle, a spherical body which is made up of (1) a central mass of dead and autolysed tissue (caseous material), surrounded by (2) a zone of proliferated histiocytes (epithelioid cells), which merges into (3) a zone of fibroblasts and lymphocytes. In the neighbourhood of the junction between (1) and (2) giant cells are generally present. There is no growth of capillaries and no polymorph reaction.

How these areas appear in any section depends on just where the section passes through the lesion and on the relative amounts of caseation and granulation tissue. When little caseation is present the tubercle is called granulomatous, and when there is much caseation it is called a caseous tubercle.

The dead tissue consists of structureless or slightly granular debris which stains pink with eosin and contains no nuclei, although fragments of nuclei may be seen in it, especially in the peripheral part. Macroscopically this tissue is firm, opaque and pale yellow in colour, and from its resemblance to cheese is called an area of caseation. The epithelioid cells are histiocytes having faintly stained cell bodies of irregular outline ; their nuclei are oval or elongated, vesicular in appearance and contain little chromatin. Many of the cells have delicate processes passing to and connecting them with their neighbours ; others may be round, oval or polygonal in shape ; they all have relatively abundant cytoplasm. Further out are the fibroblasts, and it is not always possible to distinguish young fibroblasts from epithelioid cells. The fibroblasts are scanty in young tubercles but become more numerous in older ones ; they are arranged irregularly, sometimes in a concentric and sometimes in a radial manner. Amongst the fibroblasts and still farther out is a zone of lymphocytic infiltration. The giant cells which arise from histiocytes vary greatly in size ; they are usually large, of irregular outline, and often have numerous delicate projecting peripheral processes which ramify with those of the epithelioid cells ; their protoplasm usually stains pink, and in it a few small vacuoles may be found. Their nuclei are oval and stain rather more deeply, but otherwise resemble those of the epithelioid cells. They are usually numerous and arranged round the periphery of the cell. This granulation tissue is characteristic of tuberculosis in whatever organ or tissue it may be found and whether forming isolated or conglomerate tubercles or part of a more diffuse reaction such as occurs in a tuberculous pleurisy.

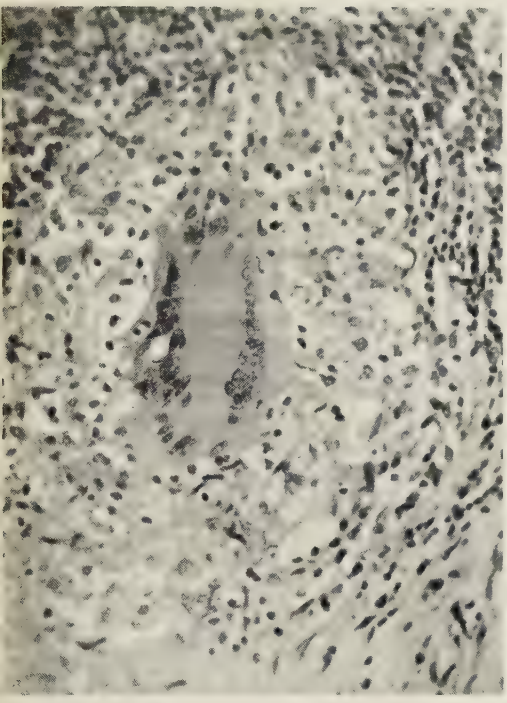
Apart from the granulation tissue the characteristic feature of tuberculosis is its tendency to caseation ; in progressive lesions the caseation spreads, more and more of the granulation tissue being killed, neighbouring tubercles frequently joining up and new granulation tissue being formed in the periphery of the old. In more acute cases the caseation spreads more quickly than the granulation tissue forms, and although a reaction consisting of histiocytes and lymphocytes may be found at the advancing borders of the caseation no recognisable tubercles may be formed. This type of tuberculosis is best seen in caseous pneumonia, and usually in this condition tubercle bacilli are present in the greatest numbers.

FIG. 62.—A giant cell forming the centre of a minute tubercle. Surrounding the cell are numerous epithelioid cells and outside these again a zone of lymphocytic infiltration. At one corner the fibrous tissue of a neighbouring tubercle can be seen. Processes can be made out joining the giant cell to the epithelioid cells and also passing from one epithelioid cell to another. The nuclei of the giant cell are arranged round the periphery ; they are well formed and mostly oval in outline. A few small and one larger vacuole can be seen in the protoplasm of the giant cell.

FIG. 63.—A miliary granulomatous tubercle in liver. In this tubercle there is very little caseous material, and fairly dense granulation tissue. There are several giant cells and in the periphery numerous lymphocytes. Many of the liver cells contain larger or smaller holes representing fat which has been dissolved out in the preparation of the specimen. (A fatty liver is a common finding in patients dying of tuberculosis.)

FIG. 64.—A miliary granulomatous tubercle in kidney. This tubercle is similar to that shown in the liver, save that it is more cellular.

FIG. 65.—Miliary caseous tubercles in spleen. The giant cells are well shown in the periphery of the caseous material. (The indistinct longitudinal lines are an artefact produced in cutting the section.)



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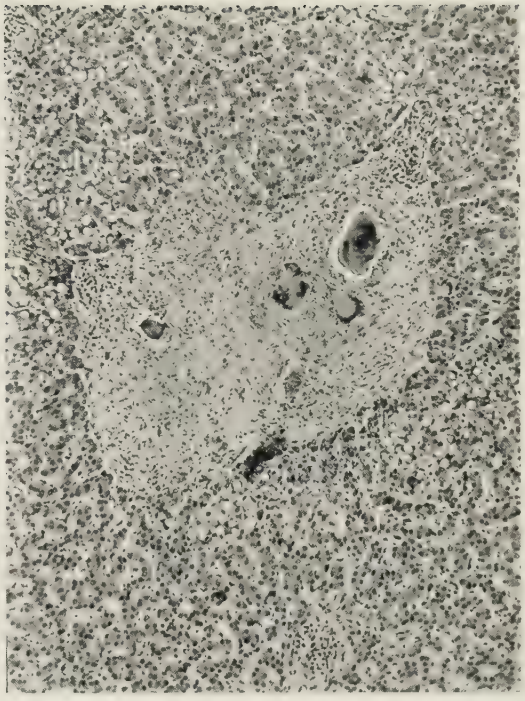

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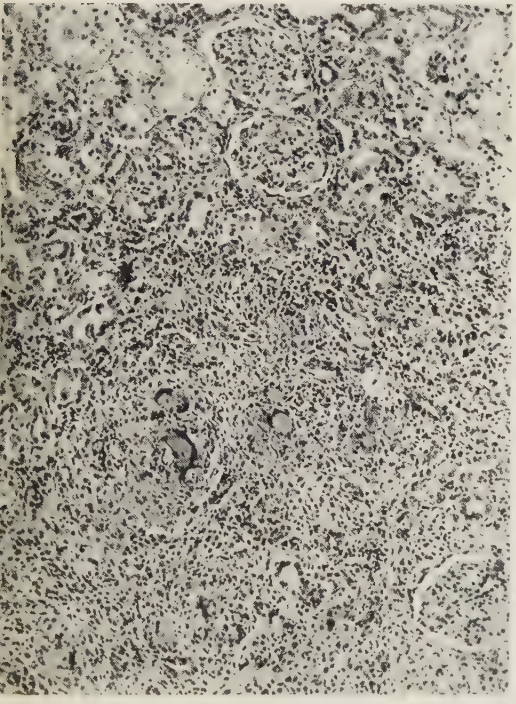
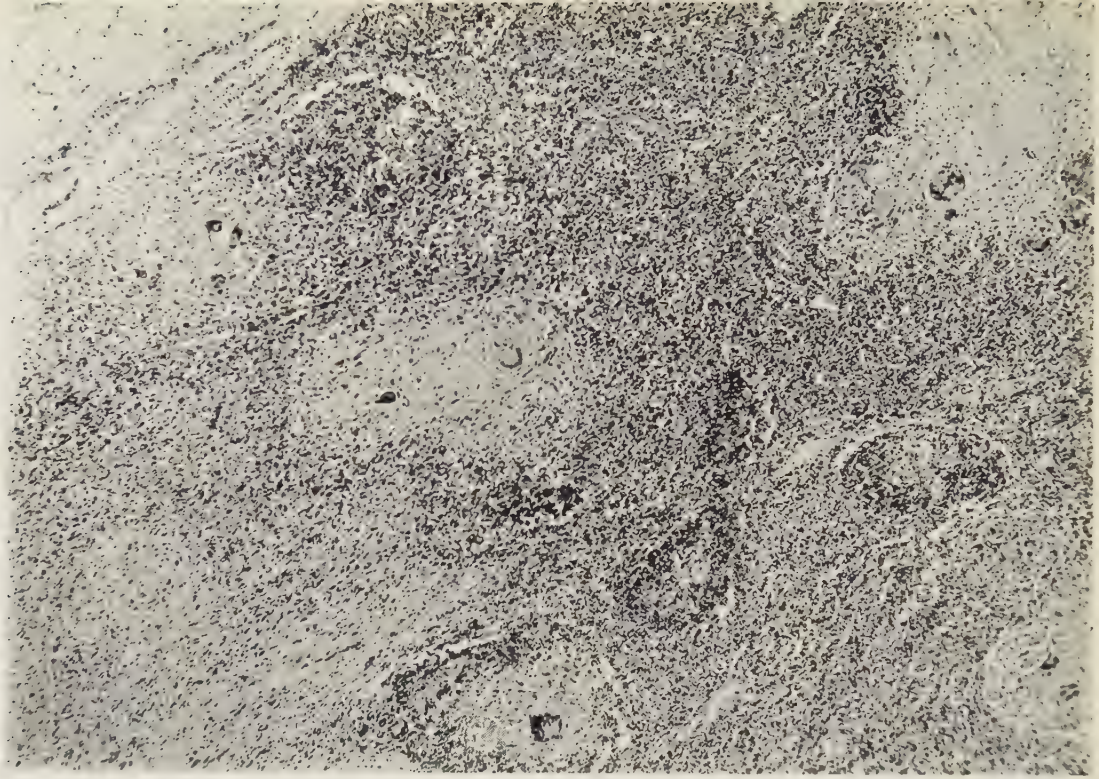


FIG. 64.

FIG. 65.



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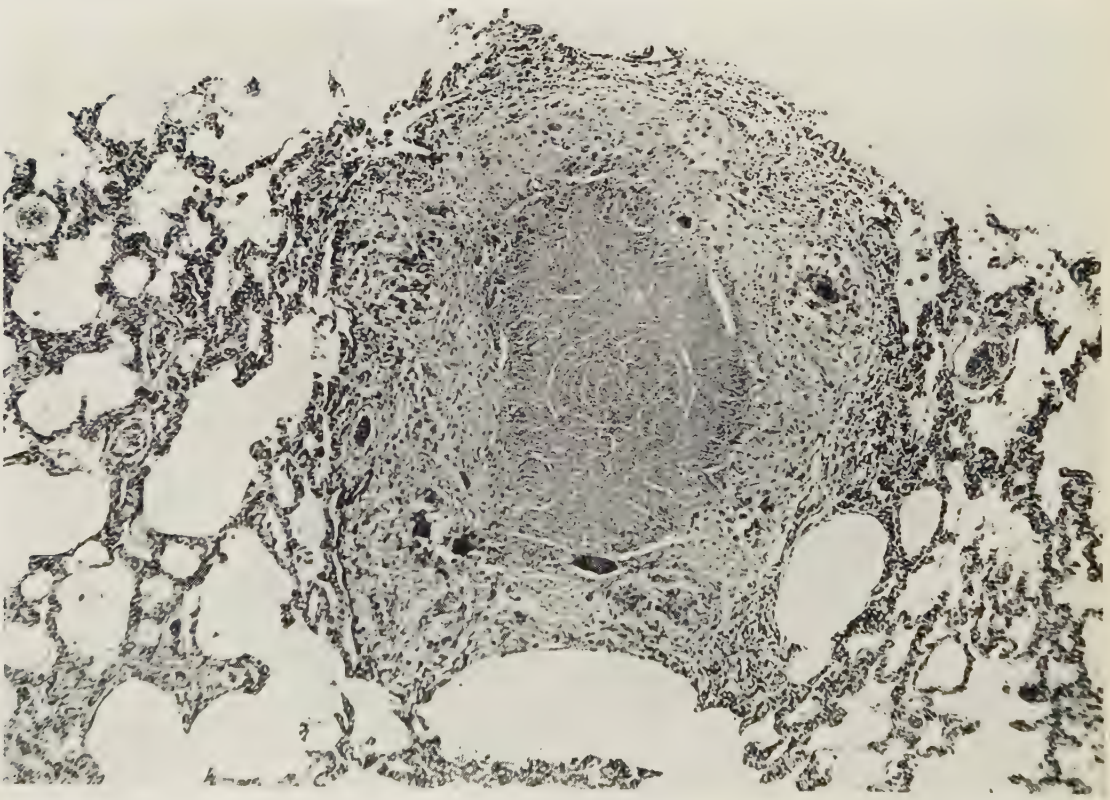


FIG. 67.

FIG. 66.—A low-power view of scattered tubercles in a lymphatic gland. They are mostly caseous, with the giant cells in the periphery of the caseous material.

FIG. 67.—A low-power view of a large tubercle in lung. The centre is caseous, and the periphery consists of epithelioid cells, fibrous tissue and giant cells. Outlines of smaller tubercles in the wall of the larger can also be made out.

FIG. 68.—Caseous tuberculosis of a lymphatic gland. In the upper part of the illustration groups of lymphocytes, small caseous tubercles and well-formed giant cells can be seen ; the lower part consists of a mass of caseous material.

FIG. 69.—Caseous tuberculous pneumonia, showing the edge of a caseous patch in lung. In the upper part the alveoli contain histiocytes, in the middle the alveolar walls can be made out, the alveoli being full of caseous material ; the lower part is occupied by a structureless caseous mass. (This lung was teeming with tubercle bacilli.)

FIG. 70.—Part of the wall of a tuberculous cavity showing the lining of caseous material and the tuberculous granulation tissue in the periphery.

FIG. 68.

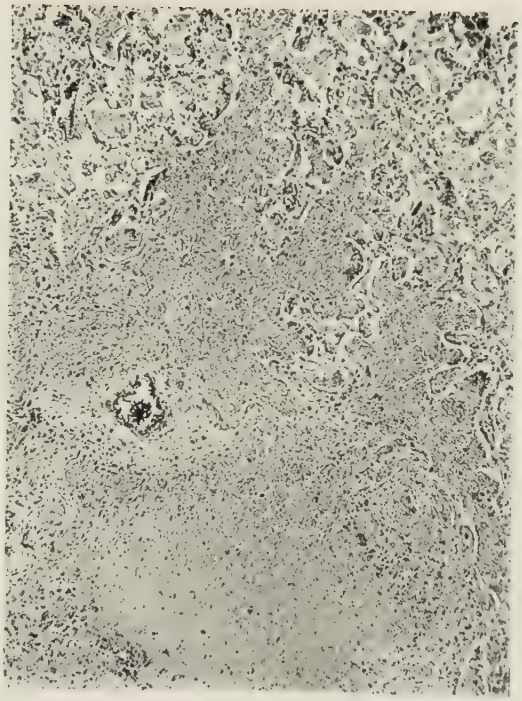
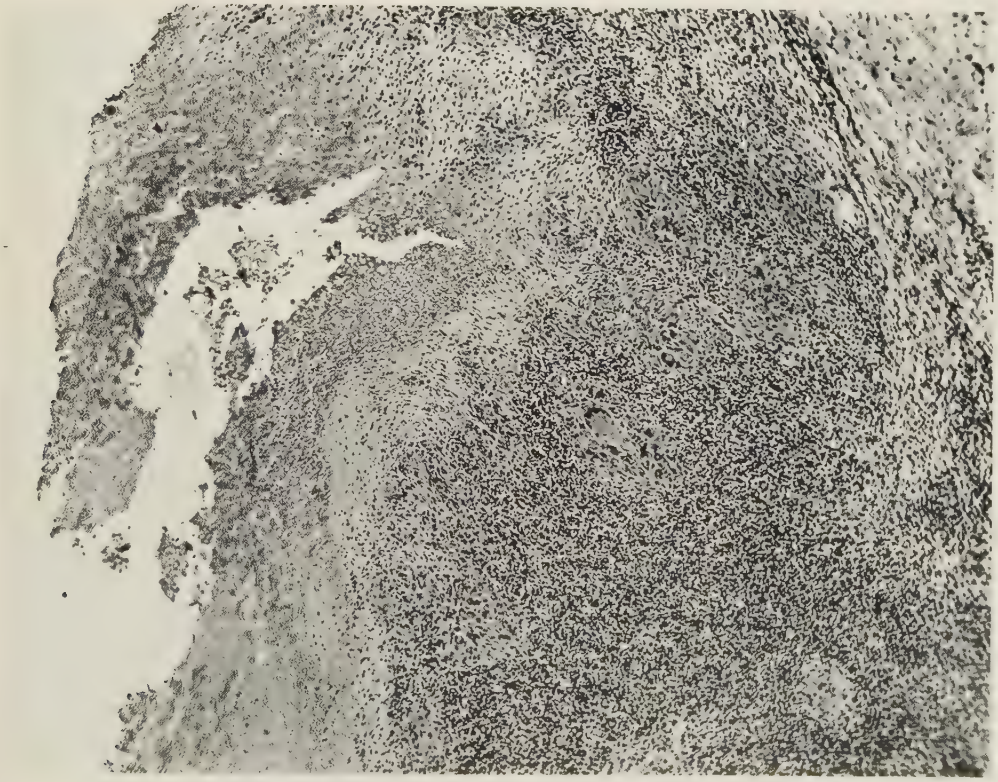


FIG. 69.



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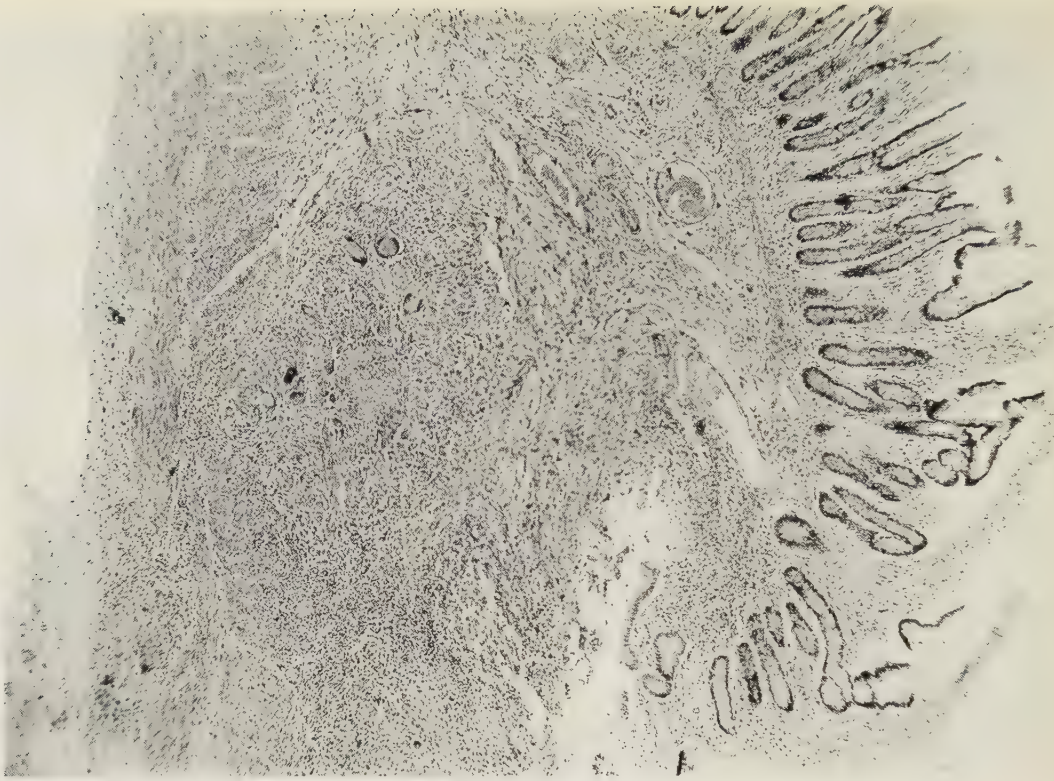

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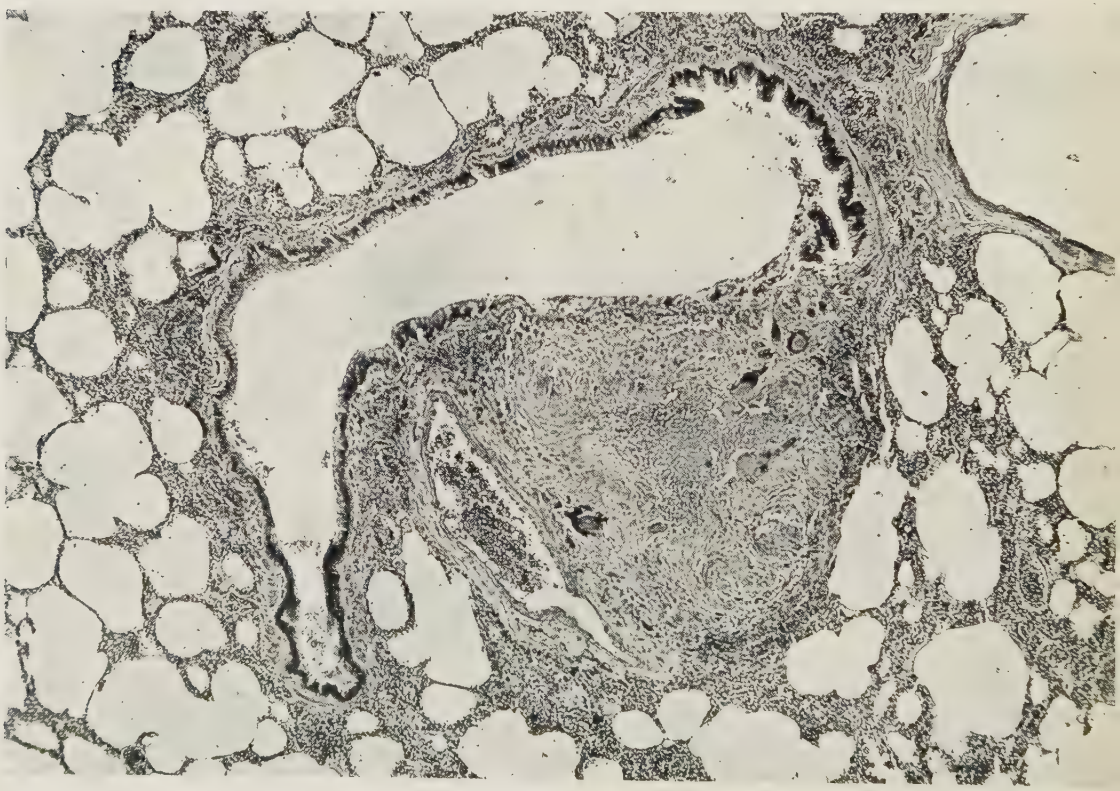


FIG. 72.

FIG. 71.—A tuberculous ulcer in ileum showing the destruction of mucosa and part of the submucosa. A group of caseous tubercles can be seen in the swollen submucosa infiltrating the muscularis, and a single tubercle in the muscularis immediately beneath the serosa.

FIG. 72.—A caseous tubercle infiltrating the wall of a bronchiole and of a vessel. The granulation tissue has reached the mucous membrane of the bronchiole and the intima of the vessel.

Syphilis

IT is rare for the junior student to be afforded an opportunity of examining a primary chancre or any of the secondary lesions histologically, so that the descriptions will be confined to tertiary syphilis.

The gumma is the characteristic syphilitic lesion ; it consists of a central area of caseation surrounded by a relatively wide zone of syphilitic granulation and fibrous tissue. The caseous material is similar to that found in tuberculous caseation, save that it sometimes shows rather more of the structure of the pre-existing but now dead tissue. The granulation tissue consists of proliferating fibroblasts, lymphocytes, plasma cells, eosinophils and occasionally giant cells. The fibroblasts tend to be radially arranged near the centre and concentrically the farther away they are from the centre. The plasma cells may be present in great numbers, but it must be remembered that they are often found in other chronic inflammations. Eosinophils and lymphocytes are most numerous in the outer zones, often collected into groups. Giant cells are not constant features of the reaction, and when present are usually small, of irregular outline and multinucleate ; they may, however, be large and indistinguishable from tuberculous giant cells. The distinguishing features of a gumma are the relatively wide zone of granulation tissue and the presence of plasma cells and eosinophils.

In recent times aortitis has become the commonest syphilitic lesion and gummata are becoming increasingly rare. The reaction begins round the vasa vasora in the adventitia and spreads into the media as a sleeve round the small vessels. In places in the media the granulation tissue spreads out to form islands which resemble early gummata but caseation is rare. The reaction in syphilitic aortitis is similar to that in the wall of a gumma, except for the fact that eosinophils are not so abundant and lymphocytes and plasma cells make up the greater part of it. Rarely a gummatous reaction is found, that is, one in which there is caseation in addition to the granulation tissue. As a result of the spread in the media the elastic fibres of which it is composed become broken up and eventually replaced by fibrous tissue.

In the wall of a gumma and rarely in the adventitia of a syphilitic aorta endarteritis obliterans is found. This is not peculiar to syphilis, as it is present in other chronic inflammations, such as tuberculosis and the base of a chronic gastric ulcer. It is, however, of diagnostic importance in some of the post-tertiary cerebral lesions.

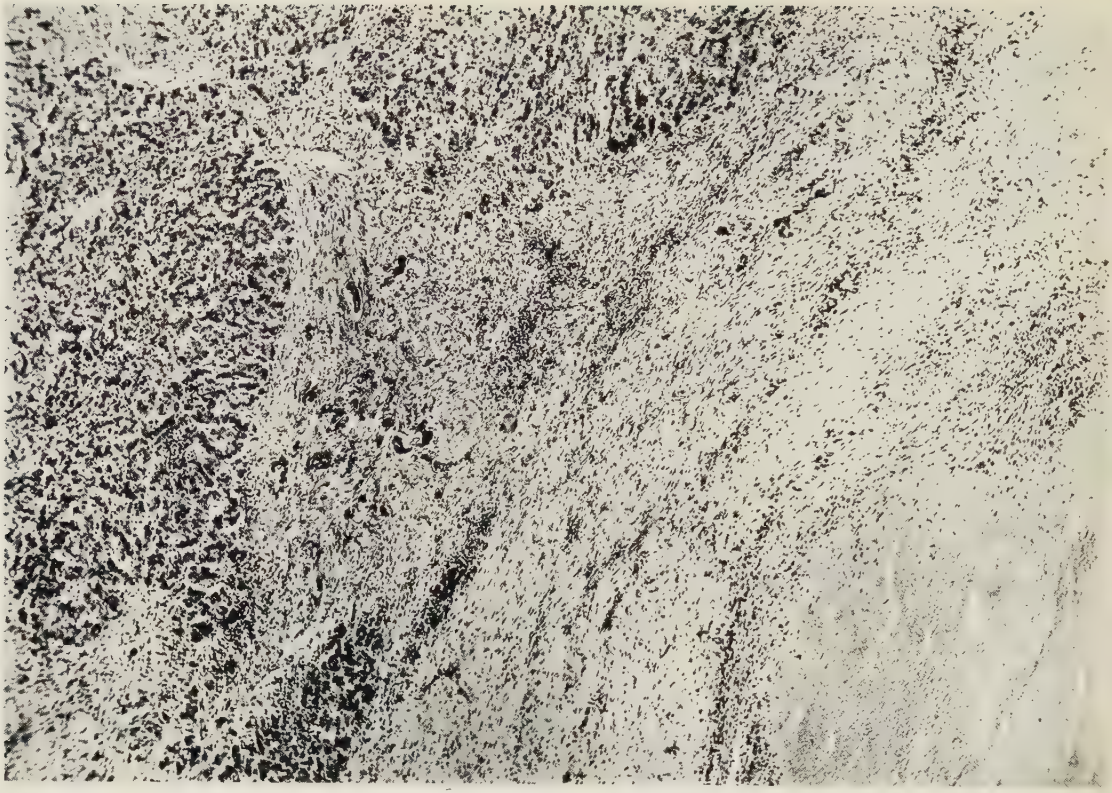


FIG. 73.

FIG. 74.

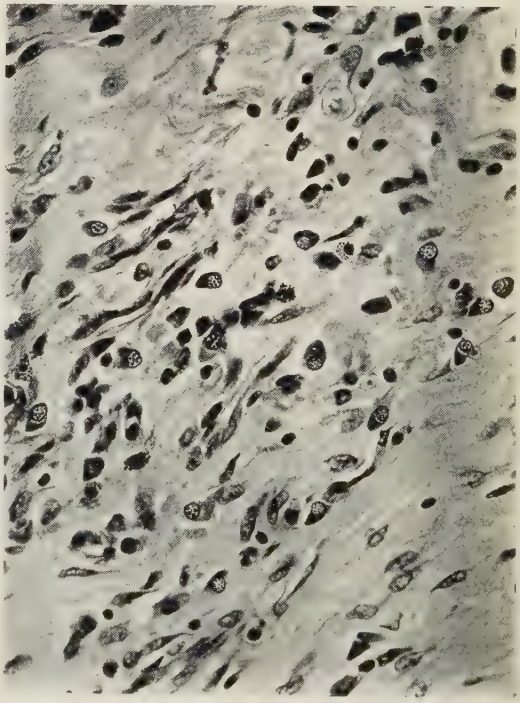


FIG. 75.

FIG. 73.—A low-power view of a gumma of liver showing the wide zone of fairly dense granulation and fibrous tissue in the periphery of an area of caseation.

FIG. 74.—Another part of the gumma shown in Fig. 73. More cellular granulation tissue surrounding the central caseous mass can be seen.

FIG. 75.—A higher power view showing the fibroblasts, eosinophil leucocytes and plasma cells of which the cellular parts shown in Fig. 73 consist.

FIG. 76.—A low-power view of the adventitia and media of a syphilitic aorta. The cellular reaction in the adventitia and spread into the media are shown.

FIG. 77.—A diagram showing the plasma cells, lymphocytes and eosinophils surrounding the vessels in the adventitia of a syphilitic aorta.

FIG. 78.—Section stained to show the elastic fibres of the media of an aorta destroyed by syphilitic granulation tissue.

Fig. 76.

Fig. 77.

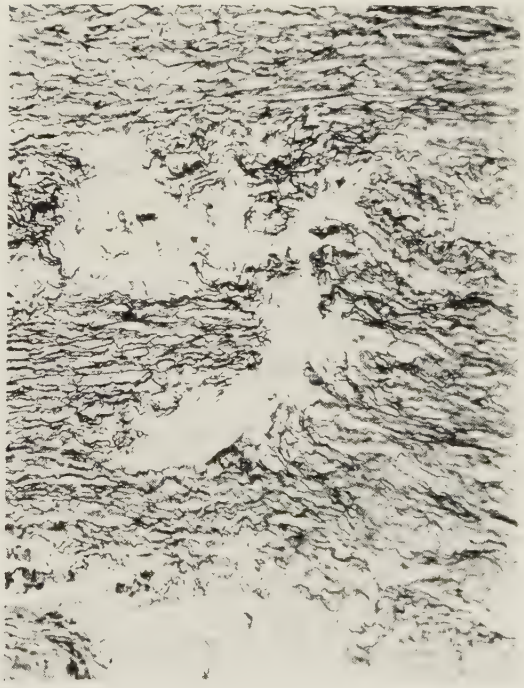


Fig. 78.

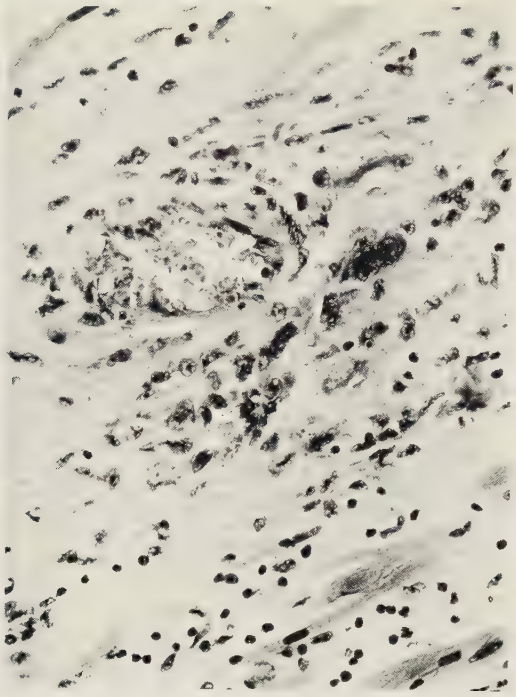
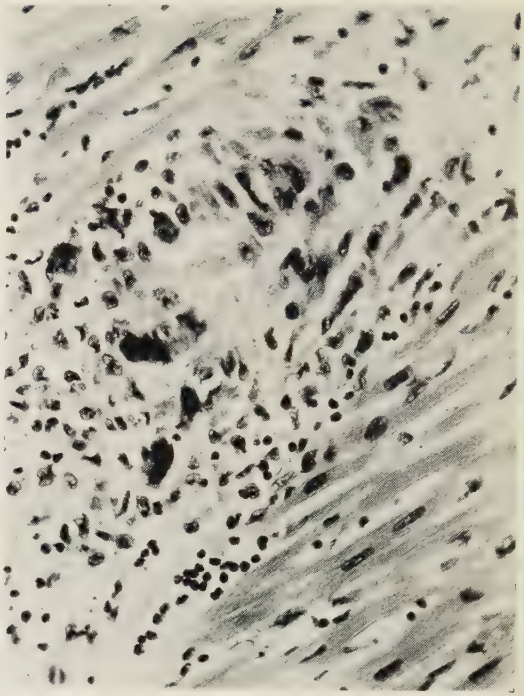


FIG. 79.



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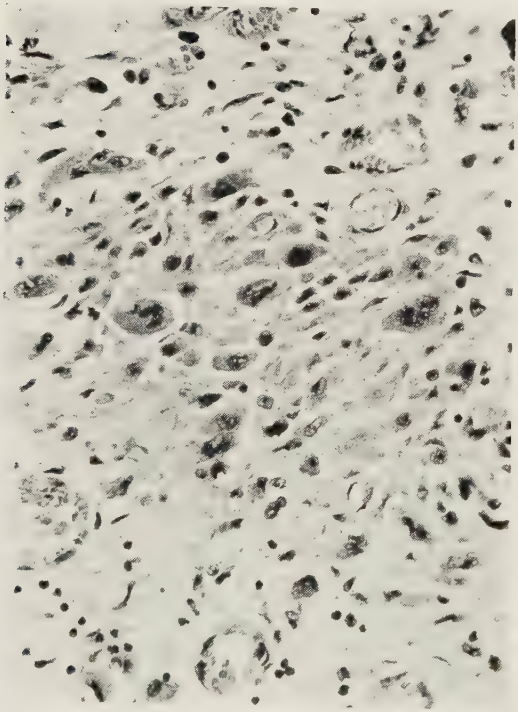

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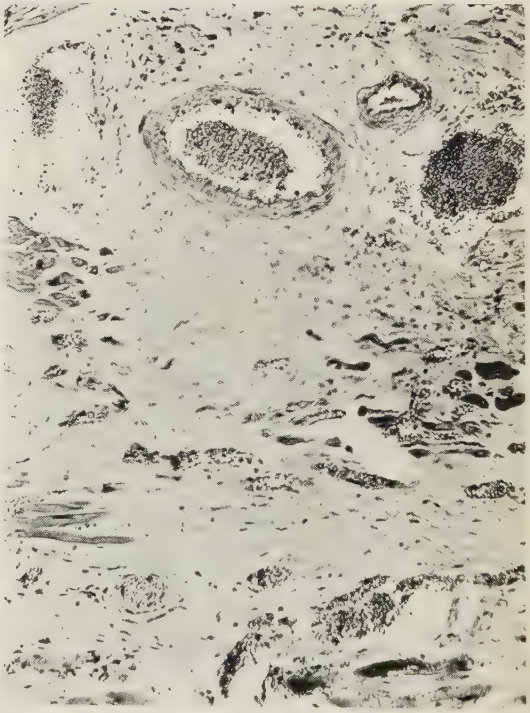


FIG. 82.

Acute Rheumatism

THE lesions produced by rheumatism are seldom available for study until the scarred or fibrotic stages are reached, and in these there is little which can be regarded as characteristic of the disease. In acute rheumatism there are usually multiple microscopic inflammatory foci in the heart with or without endocarditis and a more or less severe pericarditis. The foci which were first described by Poynton and have had special attention focused on them by Aschoff, form the most specific lesions of rheumatism. They occur most commonly in the interstitial tissue of the myocardium near a blood-vessel, and in the earliest stages consist of a few lymphocytes and concentrically arranged histiocytes. Later there is not infrequently a minute central zone of necrosis surrounded by more numerous histiocytes and lymphocytes, while eosinophils and an occasional polymorph may be present; later still the nodule is replaced by fibrous tissue. The histiocytes are large, often more or less triangular in outline, and some have one and others two or three conspicuous nuclei and abundant protoplasm.

FIG. 79.—An early rheumatic lesion near a vessel in the myocardium. The site, the large histiocytes and the slight peripheral chronic inflammatory reaction are typical of rheumatism.

FIG. 80.—A more advanced rheumatic lesion showing a small central zone of necrosis surrounded by histiocytes, two or three giant cells and a slight chronic inflammatory infiltration.

FIG. 81.—Rheumatic nodule in pericardium showing more clearly the characteristic giant cells: they are small, more or less triangular in shape, and seldom contain more than three or four nuclei.

FIG. 82.—A low-power view showing perivascular fibrosis of the myocardium in rheumatism.

Hodgkin's Disease (Lymphadenoma)

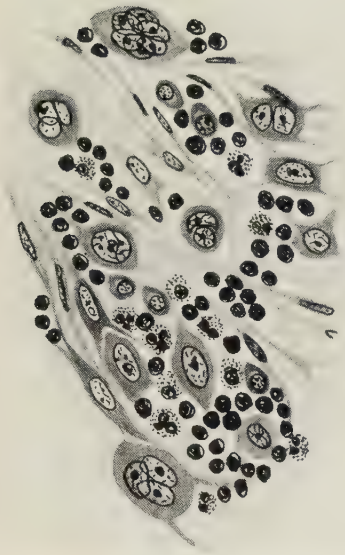
HODGKIN'S disease is a granuloma having a special tendency to affect lymphatic glands and spleen. In its very early and late stages its histological picture is obscure, in intermediate stages it is specific. It consists of a proliferation of lymphoid cells (including plasma cells), of cells forming the reticulum of lymphadenoid tissue, of endothelial cells lining lymph sinuses and of fibroblasts, associated with an infiltration by eosinophils and sometimes polymorphs. These cells make up a coherent tissue which replaces the normal architecture of lymphatic glands or forms nodules in other organs. The cells derived from the reticulum and probably from the endothelium of the sinuses constitute the most characteristic feature of the reaction. They vary in size, some being little larger than those normally forming reticulum, while others are many times as large. Their protoplasm may be homogeneous or reticulated and their outline well defined, except for slender processes which pass from some of them and anastomose with other fibres in their neighbourhood. They contain one or more nuclei, which may be round, oval or kidney-shaped, have a distinct outline and chromatin net, and one or sometimes two conspicuous nucleoli. Eosinophils are nearly always present, but vary greatly in number; polymorphs are seldom present.

FIG. 83.—A diagram of the early changes in Hodgkin's disease. Hodgkin's giant cells, eosinophils, plasma cells, lymphocytes and fibroblasts can be seen.

FIG. 84.—A diagram of the late changes in Hodgkin's disease : the great fibrosis, scattered eosinophils and lymphocytes and giant cells are shown.

FIG. 85.—Active Hodgkin's disease of lymphatic gland. The normal structure of the gland has been replaced by a tissue consisting of giant cells, fibroblasts, eosinophils and occasional polymorphs, lymphocytes and plasma cells.

FIG. 86.—Active Hodgkin's disease of lymphatic gland similar to the former, save that the plasma cells are more numerous and better shown.



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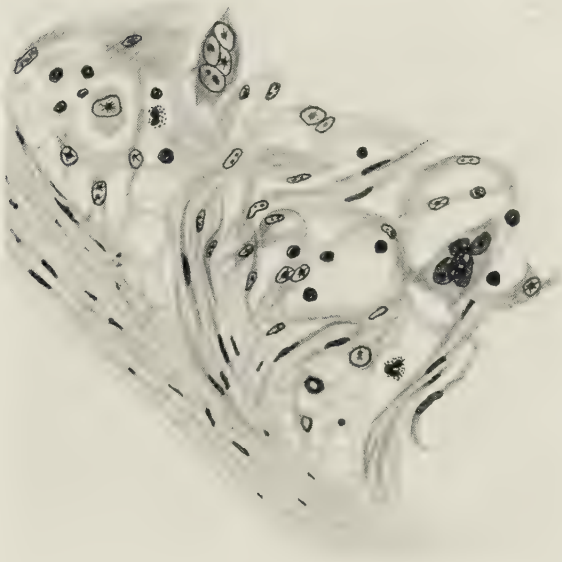

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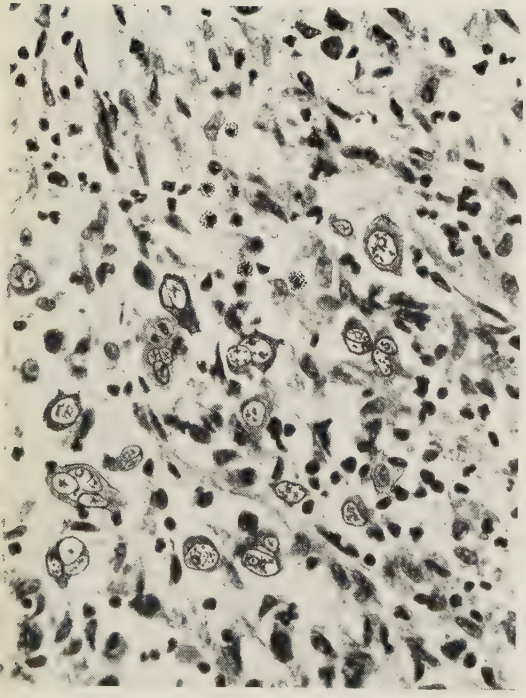

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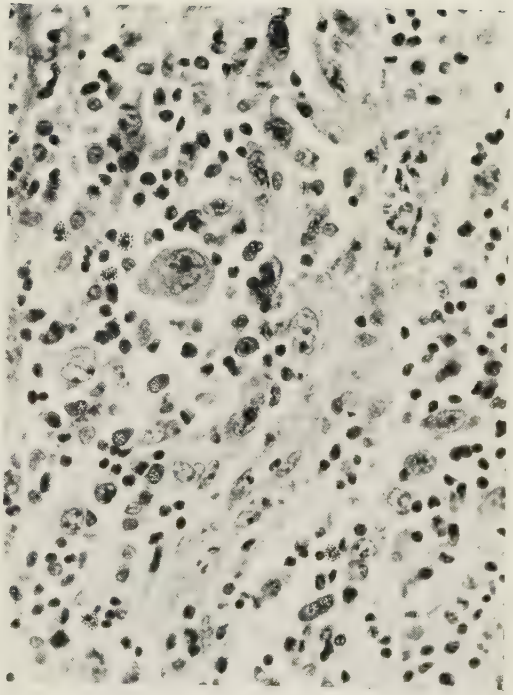

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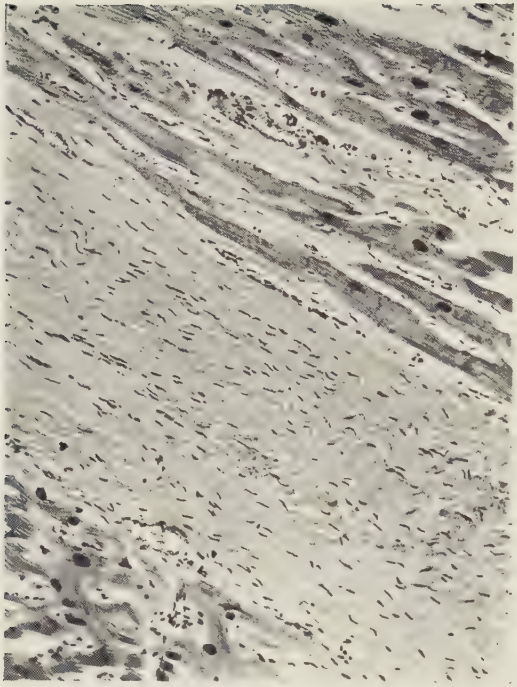

FIG. 87.

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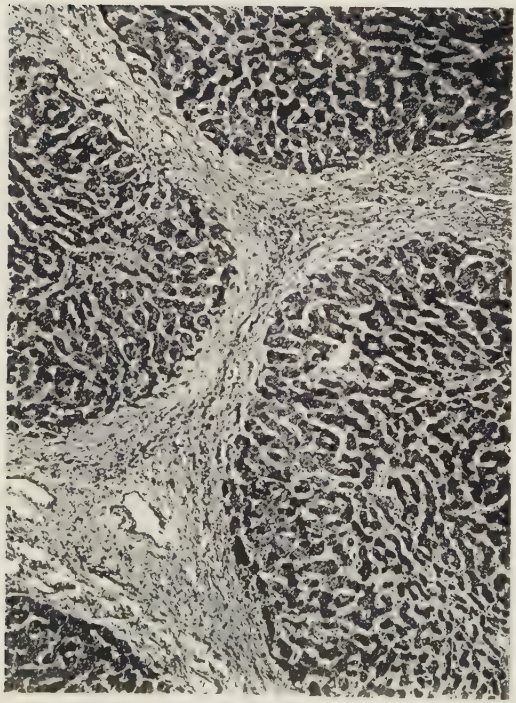


FIG. 89.

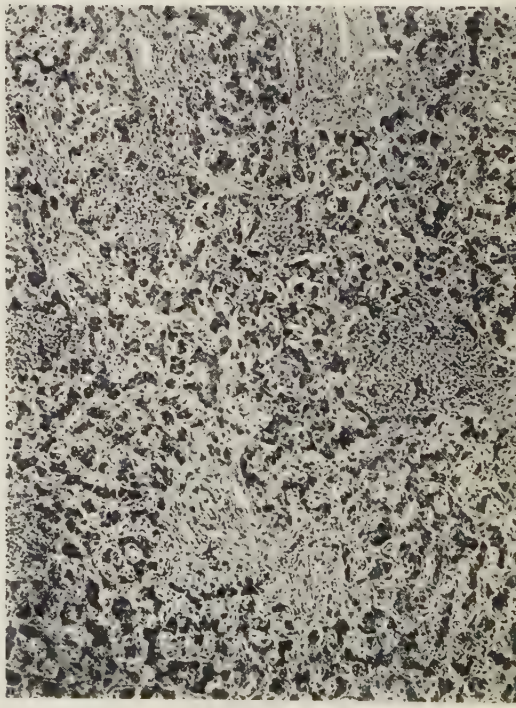


FIG. 90.

Fibrosis

THE production of new fibrous tissue may accompany or be the end result of any inflammation ; it may occur as a gradual change in which the fibrous replaces a more highly specialised tissue, or it may occur in association with tumours. Examples of fibrosis following inflammation have already been given. One of the best illustrations of the replacement phenomenon occurs in non-inflammatory fibrosis of the heart. This is a common condition in old people with degenerate arteries ; muscle bundles die and are removed by autolysis and resorption, and their place is taken by new fibrous tissue. The blood supply is apparently sufficient for the needs of the fibrous tissue but insufficient for the more highly specialised myocardium. A similar change is very common in myomata of the uterus, the muscle bundles being gradually replaced by fibrous tissue until in some cases no muscle is left in the tumour. Some carcinomata excite the formation of new fibrous tissue which makes them hard, and because of this are called scirrhous : in parts of them the fibrous tissue may greatly exceed in bulk the epithelial cells forming the essential part of the tumour. The liver is commonly the seat of a low-grade inflammation in which liver cells are destroyed and a net-work of fibrous tissue spreads through the whole organ.

FIG. 87.—Fibrous replacement of myocardium.

FIG. 88.—Dense fibrous tissue surrounding trabeculæ of carcinoma cells.

FIG. 89.—Fibrosis of liver ; comparatively acellular dense fibrous tissue is shown dividing the liver into irregular lobules.

FIG. 90.—A section of liver from a congenital syphilitic fœtus showing diffuse fibrosis and small collections of hæmopoietic cells.

Regeneration

IT has already been mentioned that when a breach occurs in the continuity of epithelium covering a surface it can be made good provided it is not too wide. This is brought about by proliferation of cells at either edge, and these grow out as a thin sheet to cover the denuded area. If for any reason there should be delay in healing the epithelium gets heaped up at the margins, and until the inflammatory reaction has reached the healing stage it will not recover the surface. In the skin the epithelium can make good wide areas of destruction, but it is only the epithelium that re-forms, the appendages of the skin, hair follicles, sebaceous and sweat glands do not. The mucous membrane of the stomach and intestine proliferates in the same way, growing as a thin sheet of cells, and from these tubular downgrowths sprout to form the appropriate glands. In glands regeneration of the parenchyma takes place by multiplication of surviving cells which reproduce perfect gland tissue. The power to do this, however, is limited : if all the cells of a kidney tubule are killed it collapses and the glomerulus atrophies, in the same way if a whole lobule of liver dies it is not re-formed. So that in glands the cells of the gland unit can only make good loss in the unit and not in the gland as a whole. The parenchyma of the liver has an exceptional power of regeneration which is not confined to the hepatic cells but is shared by those lining bile ducts. This is well illustrated in examples of non-syphilitic cirrhosis, which is a condition in which liver cells are destroyed and a chronic inflammatory and fibrous tissue net-work spreads through the whole organ. In a typical example cell groups survive in the majority of lobules, and these proliferate, forming regeneration nodules of varying size. The nodules are composed of columns of well-formed liver cells, but fail to reproduce the normal structure of the lobule, the regular relations to central and portal veins, hepatic arteries and bile ducts being lost. In advanced cases the normal architecture of the liver is replaced by a disorderly collection of islands of liver cells showing no uniformity in size, shape or blood supply. The cells of the bile ducts also proliferate, producing great numbers of immature canaliculi which lie scattered in the connective tissue. Nodules of liver cells are to a limited extent produced by these proliferating ducts.

FIG. 91.—A diagram of healing ulcer as seen with a low power. The epithelium has spread over the ulcer as a thin sheet, while at the edge it has grown down in an irregular manner. The irregular downgrowth of the epithelium is a characteristic feature of delayed healing.

FIG. 92.—The floor of a healing gastric ulcer showing the epithelium re-covering it as a single layer of columnar cells. At either side small tubular downgrowths can also be made out.

FIG. 93.—A regeneration nodule in a fibrotic liver. The nodule is composed of liver cells arranged in columns, but there is no vein in the centre, nor portal systems at the periphery ; there are, however, very numerous bile ducts in the connective tissue round the nodule.

FIG. 94.—Fibrosis of liver : dense fibrous tissue, a well-marked cellular reaction and an island of liver cells having no central vein nor proper supply of blood-vessels and bile ducts are shown.

Fig. 91.

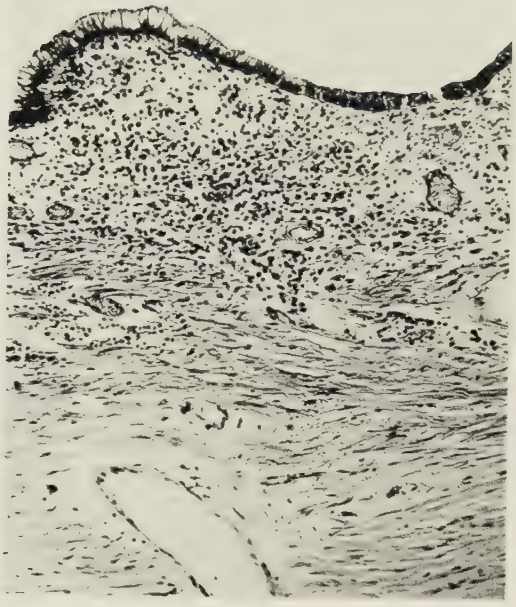


Fig. 92.

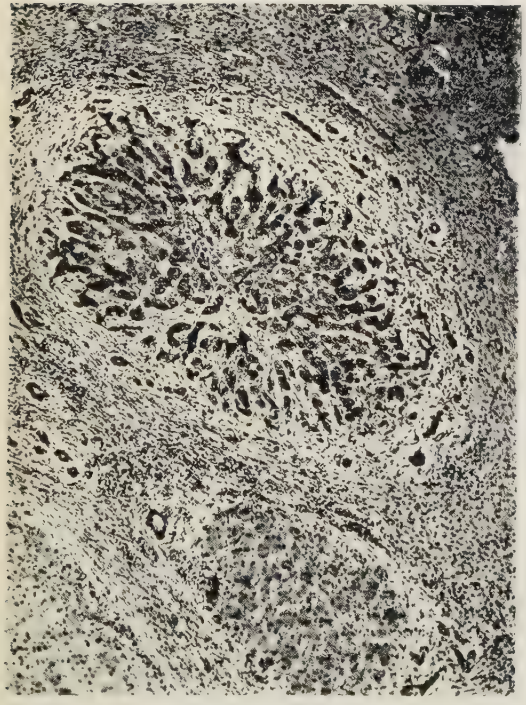
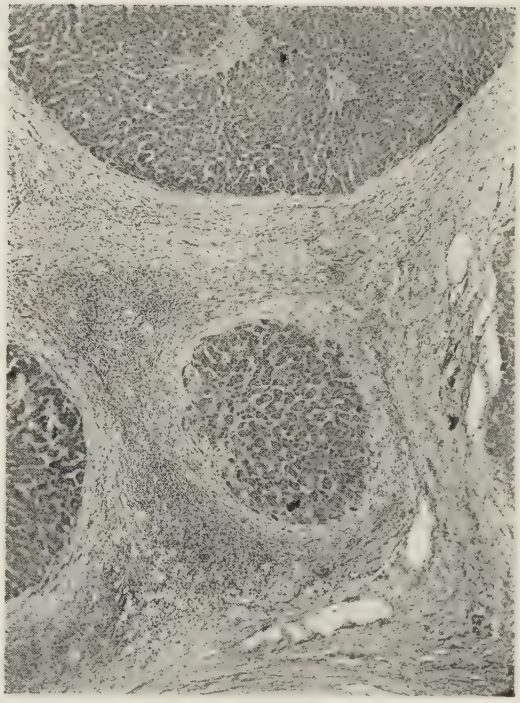


Fig. 93.



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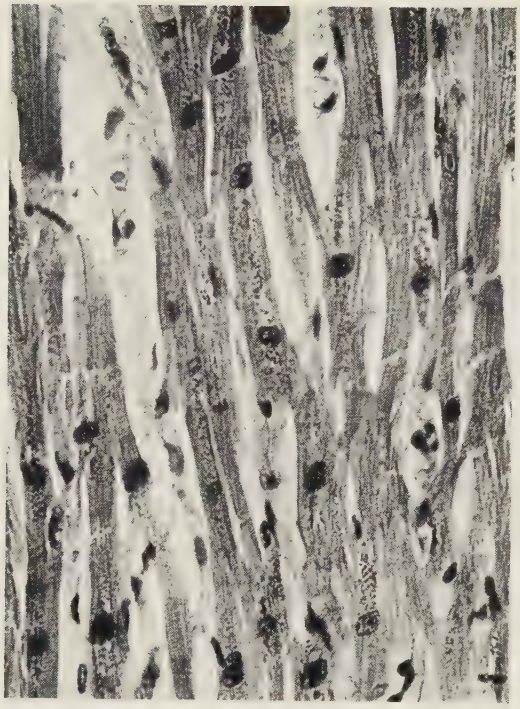


Fig. 95.

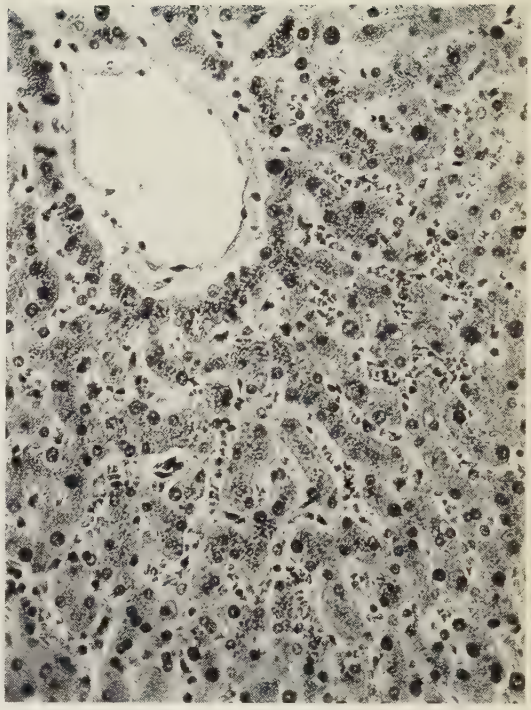


Fig. 96.

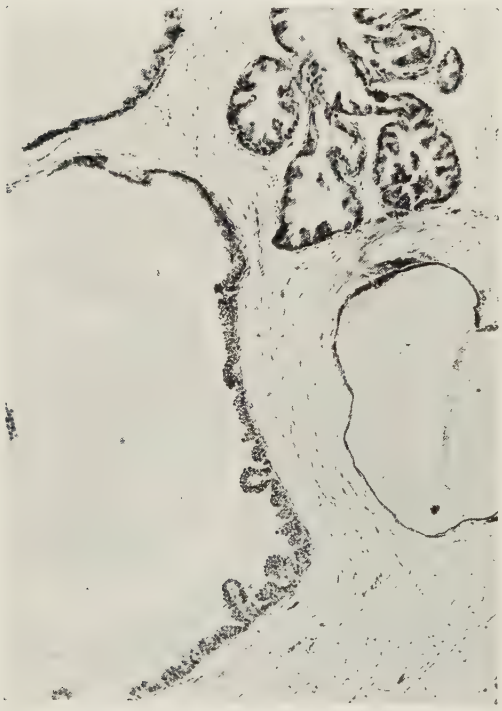


Fig. 97.

Fig. 98.

Atrophy, Hypertrophy, Hyperplasia and Metaplasia

ATROPHY means a diminution and hypertrophy an increase in size of cells without any change in their number.

By hyperplasia is meant a numerical overgrowth of cells ; this may be physiological, as in a lactating breast ; or adenomatous, when the cells resemble those normally found.

Metaplasia is a term used when cells specialised in one direction are replaced by cells specialised in another. As a result of chronic inflammation columnar epithelium lining bronchi or bronchioles becomes replaced by cubical and later by squamous epithelium ; this change from a columnar-celled mucous membrane to skin-like epithelium is an example of metaplasia. Changes of this order are not uncommon sequelæ to inflammation, and may occur in any part of the body. Malignant tumours often exhibit this phenomenon ; for instance, it is not uncommon for squamous-celled carcinomata to arise from epithelium which is not normally squamous.

FIG. 95.—Atrophy of myocardium showing the shrunken muscle bundles and the conspicuous lipochrome granules at either extremity of the nuclei. (The lipochrome granules are present but inconspicuous in normal myocardium.)

FIG. 96.—Atrophy of liver showing the shrunken liver cells which also contain granules of yellowish brown pigment.

FIG. 97.—Adenomatous hyperplasia of epithelium in cysts of breast. The cysts are lined by columnar epithelium, which is in places thrown into folds making intracystic papillæ. The cells have small, deeply stained, round nuclei and pink protoplasm. (From a case of " chronic mastitis.")

FIG. 98.—Part of the wall of a dilated chronicly inflamed bronchiole showing the transition from columnar-celled epithelium to squamous. MM. Columnar-celled mucous membrane.

Necrosis

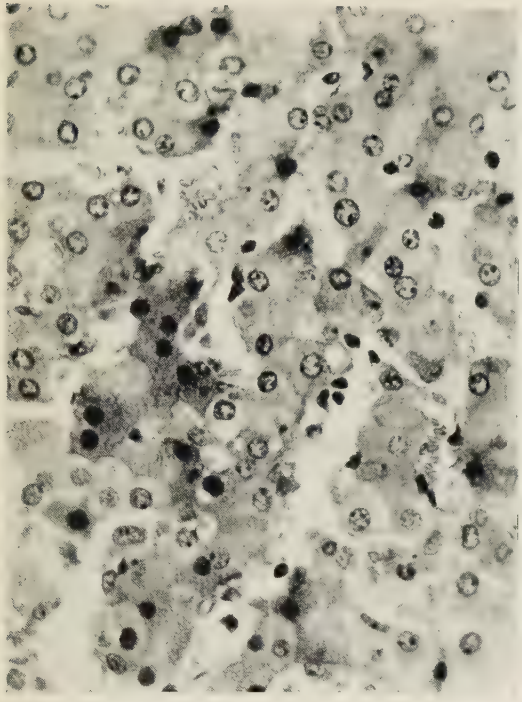
NECROSIS or death of tissue may be a final stage in a process of degeneration, or may be the direct result of an injury which kills them at once. The histological appearances by which we recognise that cells are dead are due to disintegrative changes occurring in them after their death (autolysis) and while they are still surrounded by living tissues. It is important to realise that if a group of cells or part of an organ dies, and the death of the individual follows immediately, no macroscopic nor microscopic difference will be discernible between the cells which first died and their neighbours. This is well illustrated in cases of sudden death in elderly persons due to infarction of the myocardium, the infarcted part being indistinguishable from the non-infarcted if death has been instantaneous. So that it appears that after being killed cells retain for a short time all the appearances of being alive before disintegration sets in, and when in a section a cell is referred to as being dead it is in reality in a stage of dissolution. This in the earlier stages usually consists of a swelling of the protoplasm to form a homogeneous glassy mass which stains brightly with eosin, and in the later of a liquefaction and disappearance of the cell. The nucleus at first may stain more deeply, lose its sharp outline, its chromatin break up into clumps and later the whole nucleus break up into fragments and eventually disappear, or it may retain its form for some time and then gradually fade away. The terms applied to these changes in the nuclei are pyknosis, which should mean a clumping of the chromatin, but is commonly used to mean the deeper staining of the nucleus ; karyorrhexis, which means a fragmentation of the nucleus, and karyolysis, a dissolving away of the nucleus. Small groups of dead cells are liquefied by the setting free of ferments by the cells themselves ; when larger groups die this process of clearing up is often assisted by phagocytic cells which engulf particles or even whole cells in their protoplasm. Sometimes, instead of liquefying, the dead material becomes walled off by a capsule of fibrous tissue and remains undissolved for a long time.

FIG. 99.—Pyknosis : the normal nuclei of the liver cells are well shown, and in striking contrast to them are other nuclei, which are smaller, deeply stained, structureless and some irregularly nodular.

FIG. 100.—Karyolysis in a fatty liver, the cells of which are passing on to necrosis. Many of the nuclei appear more or less normal, others have a somewhat angular outline and others have almost faded away, being represented by shadowy indistinct outlines or fragments.

FIG. 101.—A diagram of acute necrosis of liver from a case of eclampsia. The cells round the central vein are little damaged, while those farther out are dead. Between the two extremes are cells in a state of hydropic, granular, or fatty degeneration. The nuclei are ghost-like (karyolysis) in some cells, broken up in others (karyorrhexis) ; in some they appear normal, and in others they have disappeared.

FIG. 102.—Focal necrosis of liver showing normal liver cells in the periphery of a more or less fused mass of cells which have lost their outline and their nuclei. Black dots, remnants of nuclei, can be made out in some of the necrosed cells.



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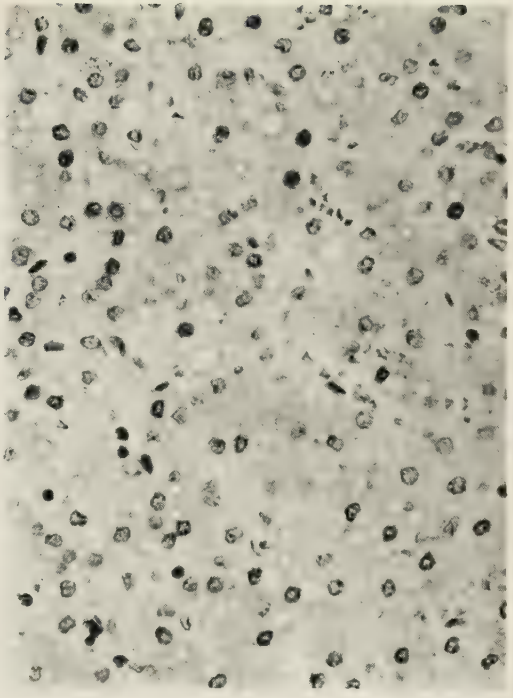

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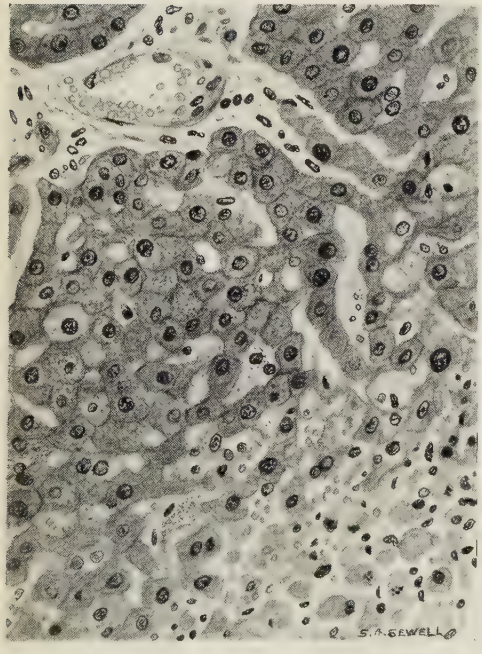

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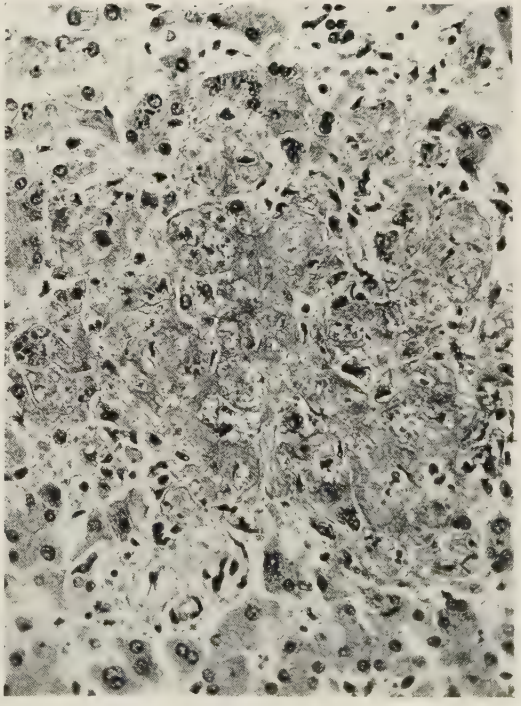


FIG. 102.

Fig. 103.

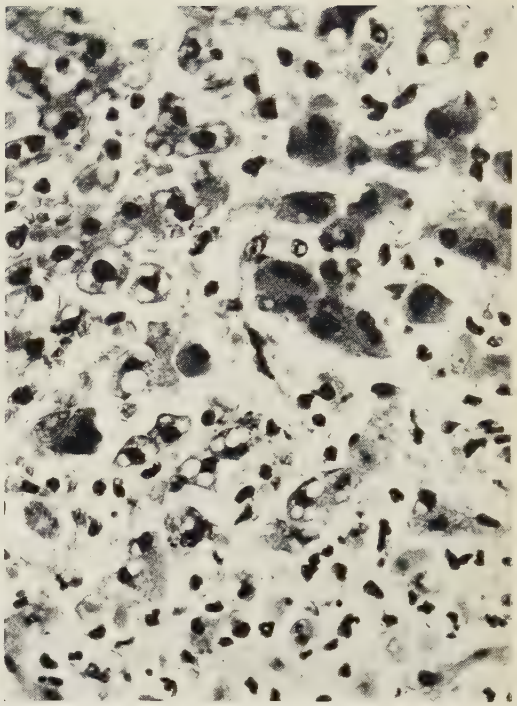


Fig. 104.

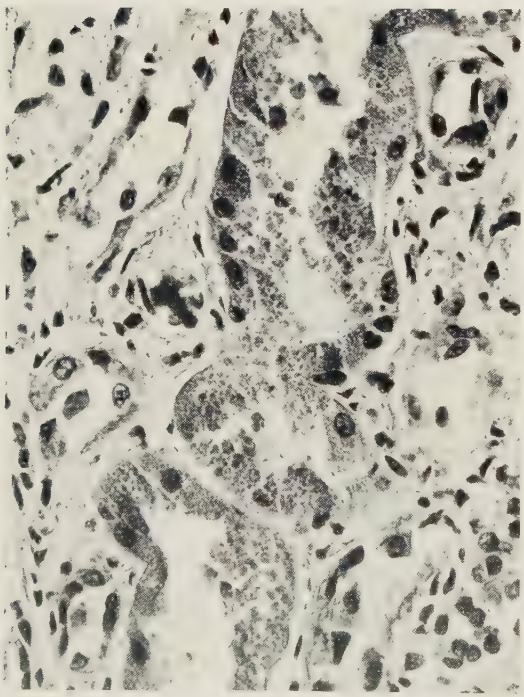


Fig. 105.

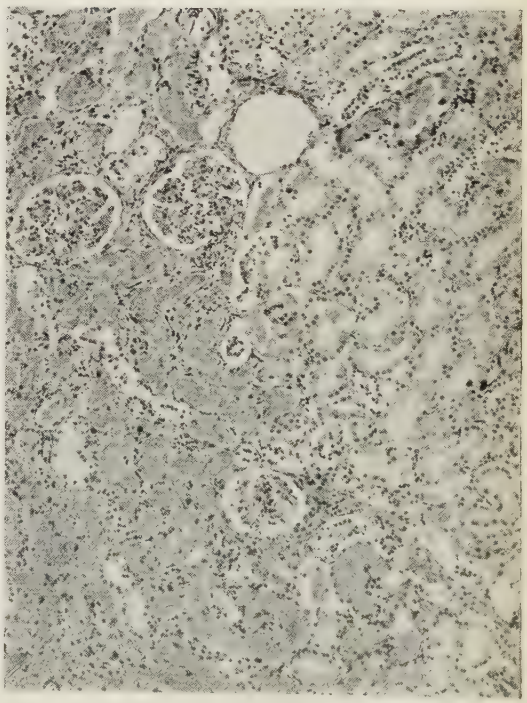


Fig. 106.

FIG. 103.—Degeneration and necrosis of liver. Many of the liver cells have lost their nuclei, in others karyolysis is obvious, and in some small circular spaces are to be made out, these being the spaces left after the fat which filled them has been dissolved out in the preparation of the specimen.

FIG. 104.—Fatty change and necrosis of liver. The nuclei are all pyknotic, many of the cells in addition to showing vacuoles are more or less disintegrated.

FIG. 105.—Hyaline granules in the cells lining tubules of a kidney.

FIG. 106.—Necrosis of cells lining kidney tubules. The dead cells have lost their nuclei and their outlines, the tubules being filled with a swollen structureless mass of pink material.

Infarcts

AN infarct consists of a localised area of degeneration or necrosis produced by interference with the circulation in the part affected. This most commonly consists of a sudden occlusion of a vessel ; if of a vein the infarct will be stuffed with blood, if an artery is obstructed the necrotic part is at first engorged, but as the dead cells swell they squeeze out the blood until the area appears to the naked eye as swollen but anæmic. The obstruction to the vessel may result from torsion, pressure from without, disease of the wall, or thrombus or embolus in the lumen. The term infarct is usually confined to internal organs ; for instance, death of a toe or finger may be produced in exactly the same way as infarction of the whole or part of a kidney, yet custom demands that the dead toe or finger shall be called gangrenous and not infarcted. As has already been mentioned under necrosis, if the death of the individual immediately follows infarction no difference can be made out between the infarcted and non-infarcted tissues ; if, however, the infarct has been produced some time prior to death it will present characteristic appearances. These will depend on the nature of the tissue in which it occurs, on whether an artery or vein has been obstructed and whether it is infected or non-infected. A non-infected infarct produced in a solid organ like the kidney presents a classical example of coagulation necrosis, that is, a necrosis in which the normal architecture of the tissue is faithfully preserved and yet the cells are dead, their nuclei have broken up or disappeared and the protoplasm has become structureless and glassy. At the periphery of the dead tissue the blood-vessels become engorged and an inflammatory reaction develops, which gradually liquefies and brings about the resorption of the infarct ; there is also a proliferation of fibroblasts which complete the healing by producing a fibrous tissue scar. The resorption is frequently incomplete, and then a larger or smaller area of dead tissue will be found encased in fibrous tissue.

An infected infarct differs from a non-infected in that from the start an intense inflammatory reaction is found in its borders. This often completely separates the living from the dead tissue, and in the late stages becomes indistinguishable from an abscess.

In the brain an infarct usually consists of an area of softening and liquefaction ; this is called colliquative necrosis.

When infarction follows the blocking of a vein the infarcted area frequently becomes so filled with blood that the outlines of the tissue and cells are lost.

FIG. 107.—Edge of infarct of kidney showing normal kidney, zone of engorged capillaries, hæmorrhage and reaction, and dead kidney.

FIG. 108.—Central part of infarct of kidney showing the preservation of the general architecture of the kidney although the cells themselves are dead.

FIG. 109.—Infarction of myocardium showing infiltration of dead muscle by leucocytes.

FIG. 110.—Infarction of myocardium showing replacement of muscle bundles by fibrous tissue.

Fig. 107.

Fig. 108.

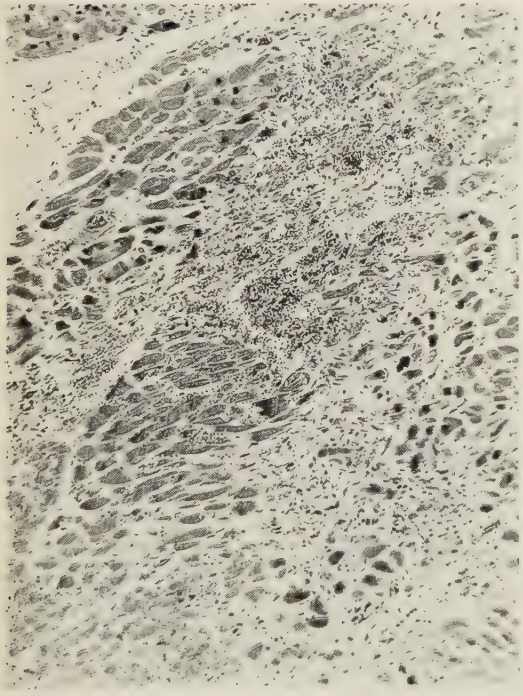


Fig. 109.

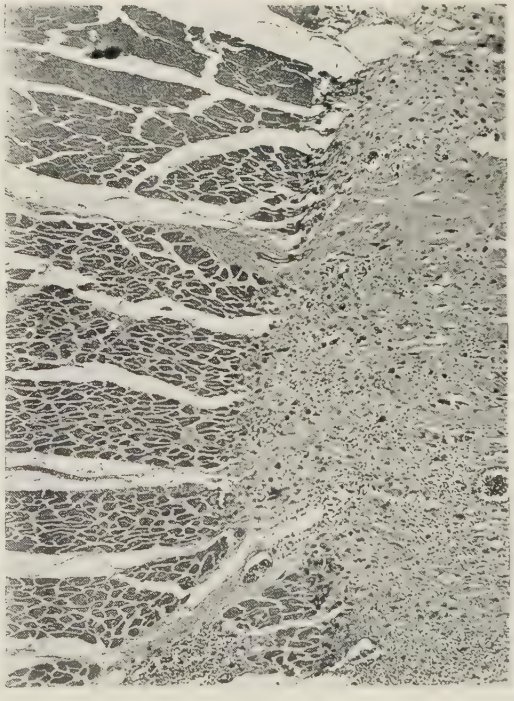


Fig. 110.

Degeneration

THIS term is used to indicate the effect of an injury sufficiently serious to bring about recognisable changes in a cell but insufficient to cause its death. The changes are most evident in the protoplasm ; the nucleus may stain more deeply than it normally does, but if it should disappear or break up into granules, the change has passed to necrosis, since a cell without a nucleus is a dead cell.

Cloudy swelling or parenchymatous degeneration is the commonest and possibly the mildest form of degeneration. In it the cells are swollen, often of irregular outline, and their protoplasm is coarsely granular. The condition affects the liver and myocardium, but is best seen in the kidney, where the cells may be so swollen as almost to obliterate the lumen of the tubules and their free edges are ragged and irregular. The granules give a positive xanthoproteic reaction and are soluble in alkalies and acetic acid, so that they consist in part, at least of protein.

Fatty degeneration is a condition in which fat can be demonstrated in cells which do not normally contain it in demonstrable form, and is to be distinguished from adiposity, a condition in which there is an excess of fat in cells that normally store it. To demonstrate fat it is usual to cut sections on the freezing microtone as the fat is dissolved out in the preparation of the specimen for impregnation with paraffin. The abnormal presence of the fat in the cell may be due to an injury of sufficient severity to prevent its utilisation, with the result that it accumulates. Or the injury may be so severe that fat which has already been built up into its protoplasm by the activity of the cell is again released in a stainable form, in which case it will be readily realised that if more fat is brought to the cell it will merely accumulate, resulting in a combination of the two processes. This combination is particularly common in the liver. The fat when present may be in the form of multiple droplets in the protoplasm, or the cell body may be distended by a single globule of fat, the nucleus being squashed against one wall. The distribution is seldom even ; in some fatty livers the cells round the central vein, in others those in the periphery of the lobule, while less commonly the cells between these two positions are most severely affected.

Hydropic degeneration is a common form of degeneration in which the cells affected appear to be blown out but empty, or have irregular vacuoles in their protoplasm. The cells remain angular and the vacuoles are not necessarily round, thus differing from fatty changes, from which it can be differentiated by

the examination of sections cut on the freezing microtome, when it will be found that even if fat is present it does not correspond in position to the vacuoles. It occurs most commonly in the epithelial cells of the kidney and liver, being especially common in the latter in chronic passive congestion.

Hyaline degeneration is a term used to include a number of unrelated conditions which have only one feature in common, namely, the presence of a homogeneous translucent material that stains brightly with eosin.

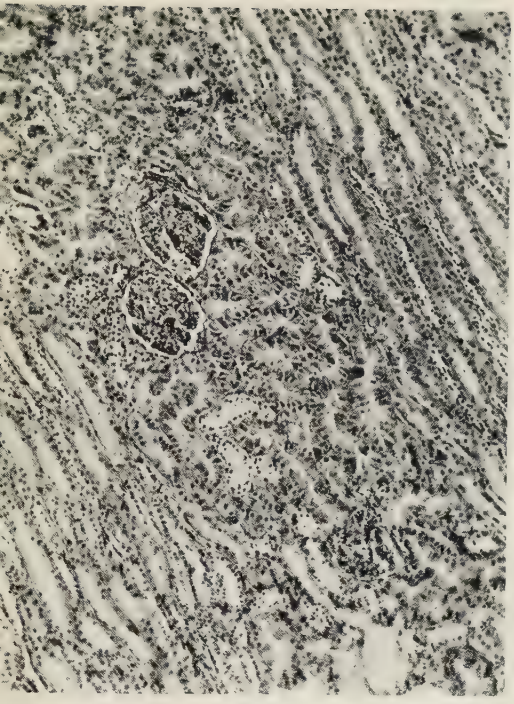
When the nature of the substance is known or when it has specific staining reactions it is no longer included in the hyaline group ; for this reason, degenerations associated with the presence of amyloid, colloid and glycogen are not included under hyaline degeneration. Apart from these, hyaline material occurs most commonly in connective tissues, in the lumen of vessels and tubules and as granules in epithelial cells. Hyaline connective tissue is common in old scars, in the walls of vessels in atrophied organs, such as uterus or ovary, in arterioles in spleen and kidneys, and in fibrous tissue in tumours. Dead muscle and glandular epithelium in the swollen stage of their dissolution also become hyaline in appearance, but do not properly belong to degeneration, and have been included under necrosis. Quite different from these are the hyaline thrombi, commonly found in capillaries, and especially in glomeruli, as they are probably composed of agglutinated red blood cells and a little fibrin. Hyaline casts in kidney tubules are made up largely of dead cells and coagulated albuminous fluid. The epithelial cells in which hyaline granules are most commonly found are those of the liver and kidney (see Fig. 105).

FIG. 111.—A low-power view of cloudy swelling of kidney showing the swollen epithelium almost filling the lumen of tubules.

FIG. 112.—A high-power view of cloudy swelling showing the granularity of the cells and their irregular outline. Some of the cells have deeply stained shrunken nuclei and others have lost their nuclei, these last having passed on to necrosis.

FIG. 113.—Hydropic degeneration of liver showing the swollen angular empty cells, many of which have lost their nuclei.

FIG. 114.—Fatty change in a kidney showing the fairly clear-cut circles in the basal part of the cells where the fat has been dissolved out in preparing the specimen.



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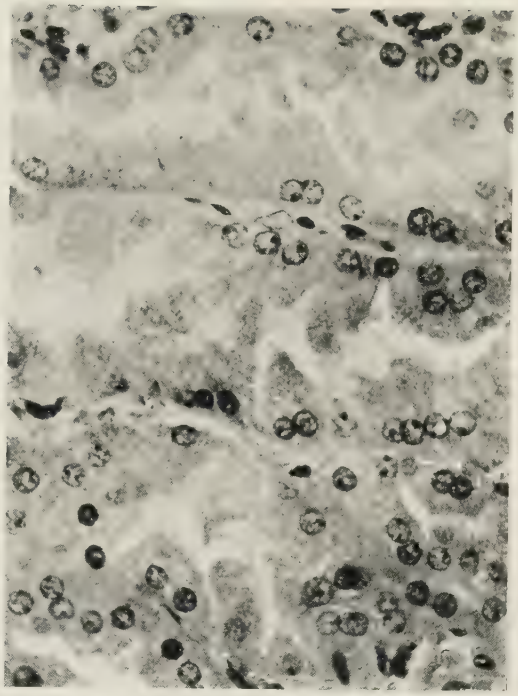
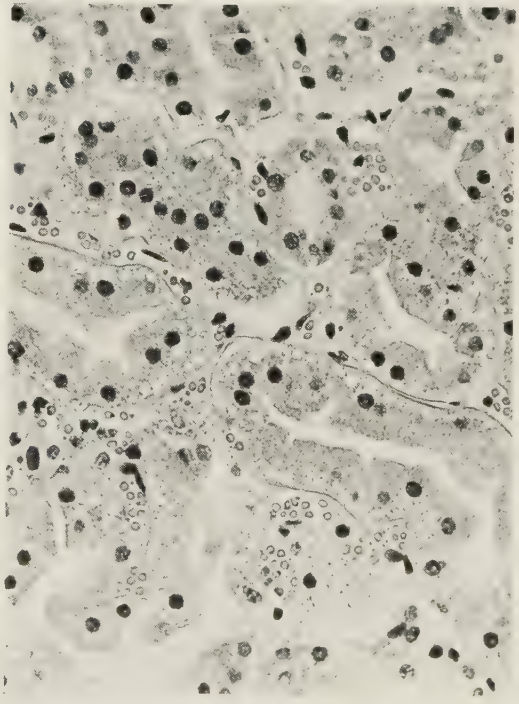


FIG. 112.

FIG. 113.



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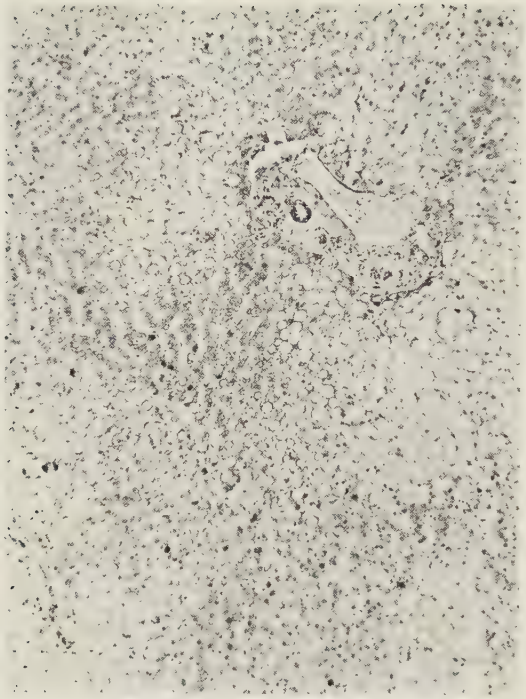

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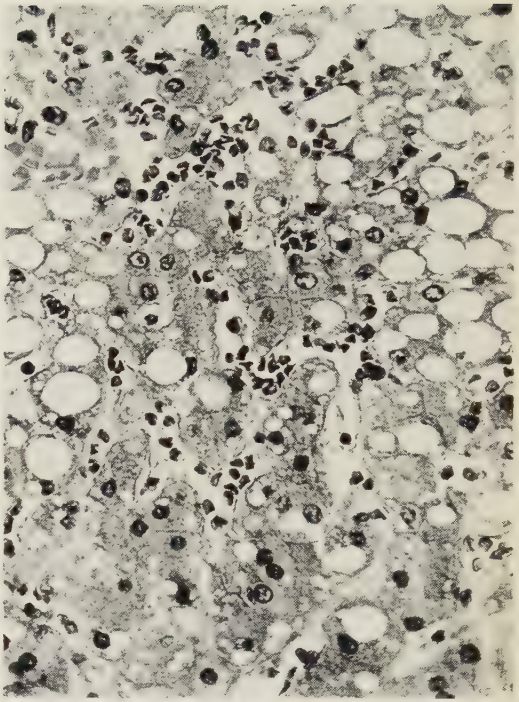

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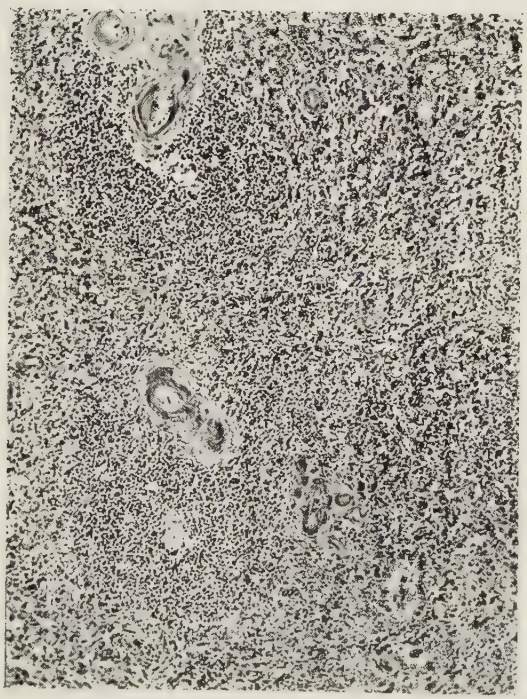

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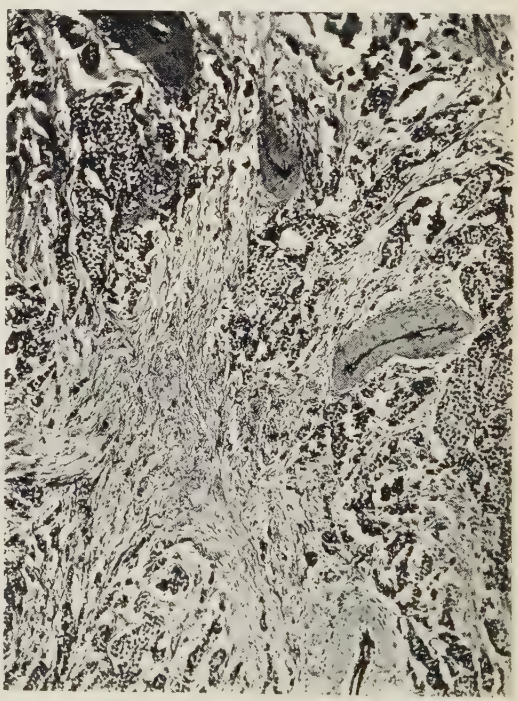


FIG. 118.

FIG. 115.—A low-power view of fatty change of a liver : the clear-cut round and oval spaces are characteristic.

FIG. 116.—A high-power view of fatty liver showing large and small spaces in the cells representing the places occupied by fat which has been dissolved out in preparing the specimen.

FIG. 117.—Hyaline degeneration of the walls of small arteries in the spleen showing the swollen homogeneous fused fibres.

FIG. 118.—Hyaline degeneration of fibrous and elastic tissue in the walls of ducts of a breast infiltrated with carcinoma.

Amyloid

AMYLOID occurs as an extra-cellular deposit, most commonly in the walls of small blood-vessels and of sinuses and sinusoids. It is commonly found in the spleen, liver and kidney: when present in them it is, however, often present in other organs, especially lymphatic glands, adrenals and mucosa of intestine. In the spleen the Malpighian bodies may be chiefly affected, or it may be diffusely infiltrated throughout. Similarly in the liver, the chief deposit may be in the walls of the blood-vessels, or it may be found as narrower or wider bands between the columns of liver cells. In the kidney glomeruli are often converted into solid structureless lumps, and the walls of the smaller vessels may also be infiltrated. In sections stained with hæmatoxylin and eosin amyloid is pink, structureless and glassy; with iodine it is brown, and with methyl-violet red. It will be realised that by its presence it is likely to interfere with the circulation in the part, and as a result the cells in its immediate neighbourhood undergo atrophy. In advanced cases this atrophy may be so great that although the actual bulk of the organ may be increased most of the parenchyma may have disappeared.

FIG. 119.—Amyloid liver showing the wide bands of homogeneous material between the columns of liver cells.

FIG. 120.—Amyloid liver showing amyloid deposited in the walls of small arteries.

FIG. 121.—Amyloid kidney showing the deposit in the glomeruli.

FIG. 122.—Sago amyloid spleen showing the deposit in the arterioles and largely replacing the Malpighian bodies.

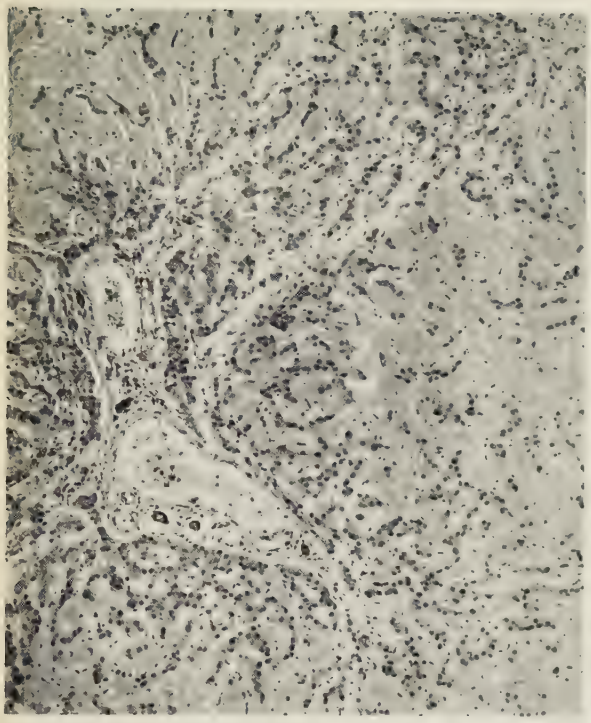


FIG. 119.

FIG. 120.

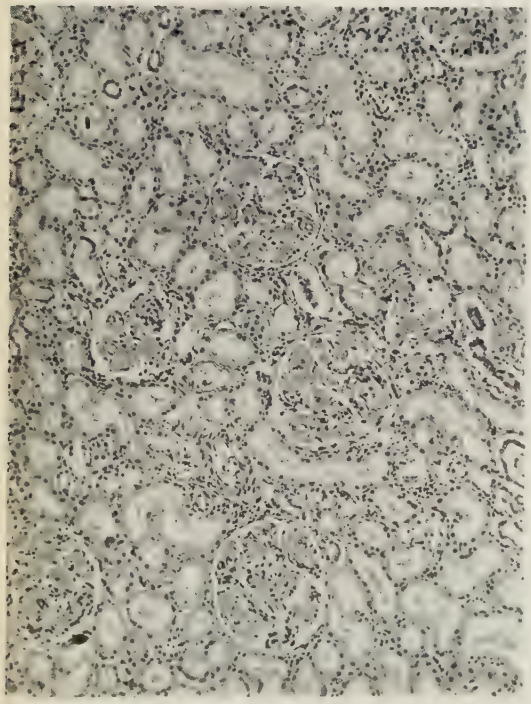
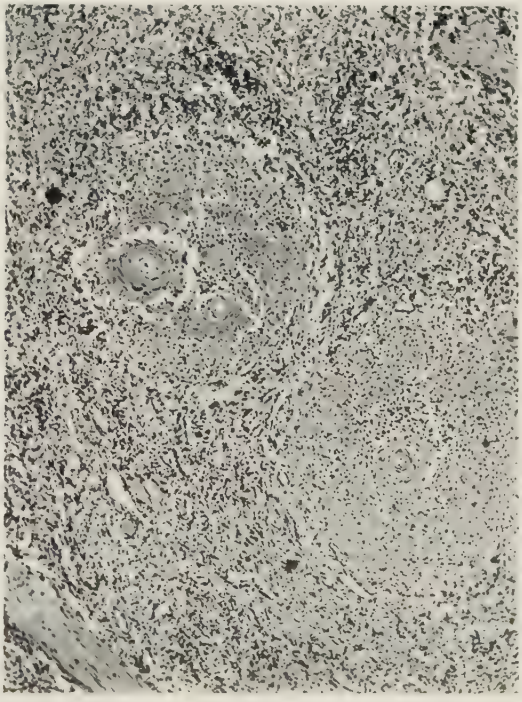


FIG. 121.



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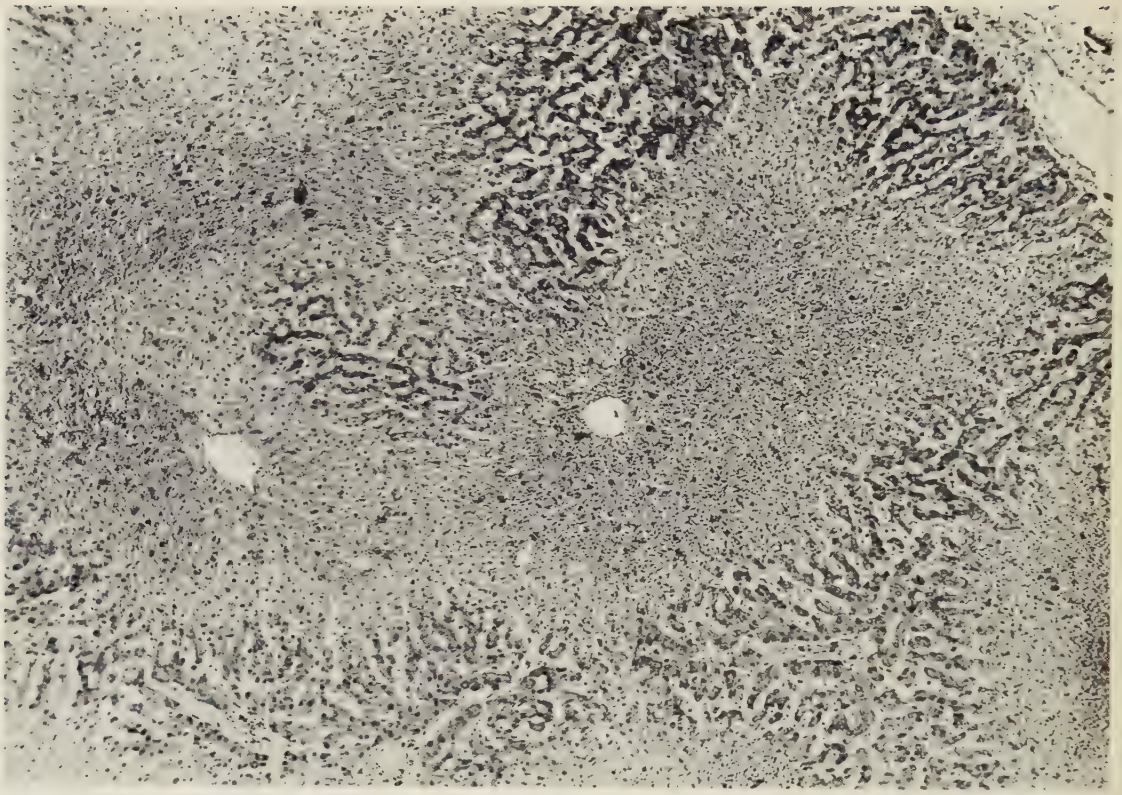

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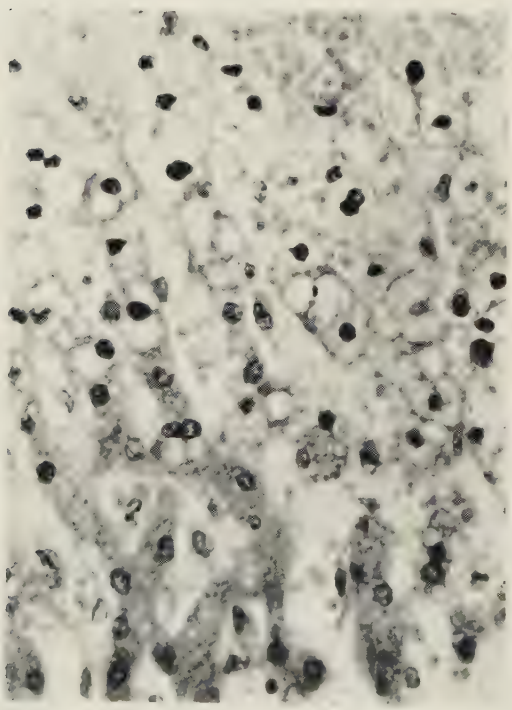

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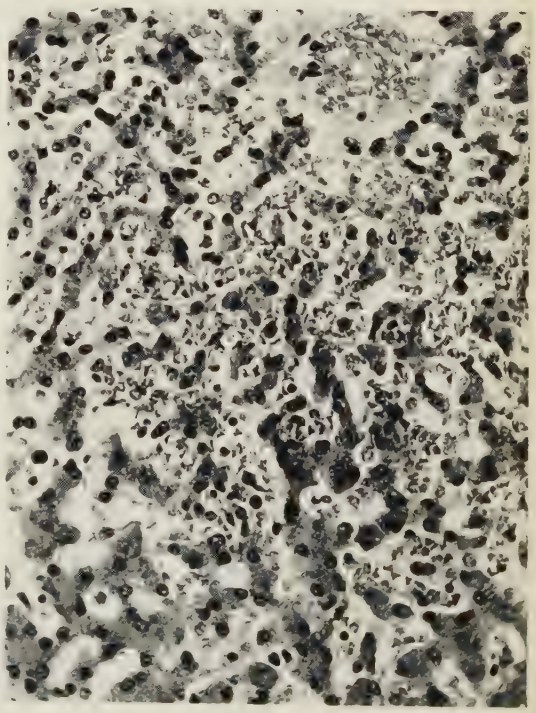

FIG. 125.

Chronic Venous Congestion of Liver

WHEN the systemic veins are over-distended for a long time, as in chronic heart failure, the liver is one of the first organs to suffer. The changes occurring in it are due to interference with the circulation of the blood in the lobules, and consist of degeneration and necrosis of cells round the central vein. In some cases fatty or hydropic degeneration precedes necrosis, in others the cells die outright. The dead cells are dissolved away and the sinusoids become engorged. This change may be so extensive that the only recognisable liver parenchyma consists of narrow zones of normal or degenerate cells round the portal systems. Sometimes the cells nearest to the central vein are found to be atrophied instead of degenerate or absent.

FIG. 123.—Passive congestion of liver showing a general low-power view of an acute example. Round the central veins the liver cells have disappeared, allowing the sinusoids to become engorged. In the periphery of this zone of engorgement the liver cells are swollen and hydropic, and in the periphery of these cells slighter degrees of degeneration are to be seen, leaving a narrow zone of normal cells surrounding the portal systems.

FIG. 124.—A high-power view of part of Fig. 123 showing hydropic and fatty cells.

FIG. 125.—Passive congestion of the liver showing congested central vein (in top right-hand corner) and sinusoids with atrophy of liver cells. The cells farthest from the hepatic and portal blood-vessels are the most severely affected.

Tumours

AT one time any lump was called a tumour ; now, however, the name is reserved for newgrowths of tissue which exhibit unlimited power of proliferation and yet never produce completed or useful organs. In this sense a tumour consists of a mass of cells which may arise in any of the tissues of the body, and which bear a close or more remote resemblance to, without being identical with, normal tissue. It is dependent on the surrounding tissues for its blood supply and fibrous tissue frame-work, and for its nourishment on the circulation of its bearer, since if the blood supply fails it dies. In all other respects it appears to be independent, and grows without regard to the well-being of other tissues or its host.

Tumours are divided into two big groups, the benign and the malignant, and these are again divided into groups according to the type of tissue of which they are composed.

Benign tumours are circumscribed, often have a fibrous tissue capsule, and the cells bear a close resemblance to those of the tissue from which they spring, though their arrangement is generally abnormal. They are frequently multiple, never infiltrate surrounding tissues, and are only inconvenient or dangerous by their position, their size or by pressure on, or other interference with, the proper function of neighbouring organs.

Malignant tumours infiltrate and destroy surrounding tissues, differ often markedly from the tissues in which they arise, metastasise, and are usually single. In the majority of cases the microscopic picture will readily reveal whether a tumour is malignant or benign ; in others it is extremely difficult if not impossible to decide which it is. Malignancy is suggested by increased cellularity, the presence of many mitotic figures, atypical arrangement or method of growth, and great variation from the normal type of cell : it is proven by metastases or infiltration. Cells of a malignant tumour (the primary), if carried to another part of the body by blood or lymph stream, or any other means, may multiply in the new situation, and so produce other tumours which are called secondaries or metastases. It is important to note that according to our present conception of malignant tumours secondaries or metastases are direct lineal descendants of cells derived from the primary, and that they cannot occur except as a result of the transport of actual cells. Round the central mass of a malignant tumour there are usually processes of cells extending out into the surrounding tissue. These outgrowths generally take the line of least resistance, and passing between

cells or along fascial planes may permeate tissues for considerable distances beyond their main mass. This method of growth by permeation is what is meant by infiltration.

The termination "-oma" is used in a general way to denote a benign, and carcinoma or sarcoma a malignant, tumour. So that fibroma, myoma, osteoma, lipoma and myxoma mean benign tumours of fibrous tissue, muscle, bone, fatty tissue and myxomatous tissue. Similarly if the termination is sarcoma it denotes a malignant tumour of these tissues. Sarcomata, however, do not always consist of differentiated tissue, sometimes only round, oval or spindle cells being found in them. These make up the group of undifferentiated, while those in which a recognised tissue is found form the group of differentiated, sarcomata. It frequently happens, particularly in tumours arising from bone, that mixtures such as osteo-chondro-fibro-sarcomata are found. The names of the epithelial tumours are not quite so straightforward : the benign are called either papillomata or adenomata, and the majority of the malignant are called carcinoma, preceded by some descriptive term. This may refer to the type of cell of which the tumour is composed, such as squamous carcinoma : to the arrangement of the cells, such as tubular carcinoma ; or to its consistence—a soft tumour being called encephaloid or medullary and a hard, scirrhous. Combinations of these terms are often used to describe the chief characters of a tumour in the fewest possible words, such as tubular, cubical celled, scirrhous carcinoma.

FIG. 126.—Squamous-celled carcinoma showing very great irregularity in size and shape of cells, giant nuclei and multi-nucleate cells. The size of the cells should be compared with the normal fibrous tissue nuclei in the bottom left-hand corner.

FIG. 127.—Another part of the tumour illustrated in Fig. 126 showing the bizarre cells, including large, irregular, multinucleate giant cells.

FIG. 128.—Large octopus-like multinucleate giant cells in a squamous-celled carcinoma.

FIG. 129.—A nodule of secondary carcinoma from femur. The primary was in thyroid, and the section shows recognisable acini containing colloid, thus forming a good illustration of a definitely malignant tumour in which the variation from normal is not very marked.

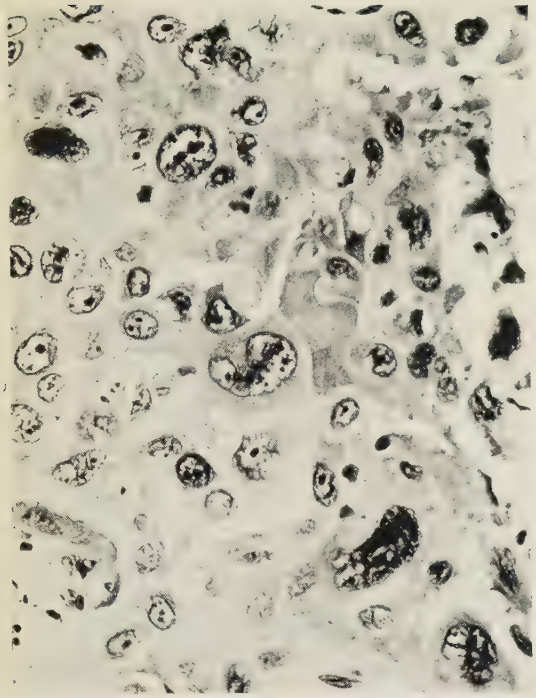

FIG. 126.

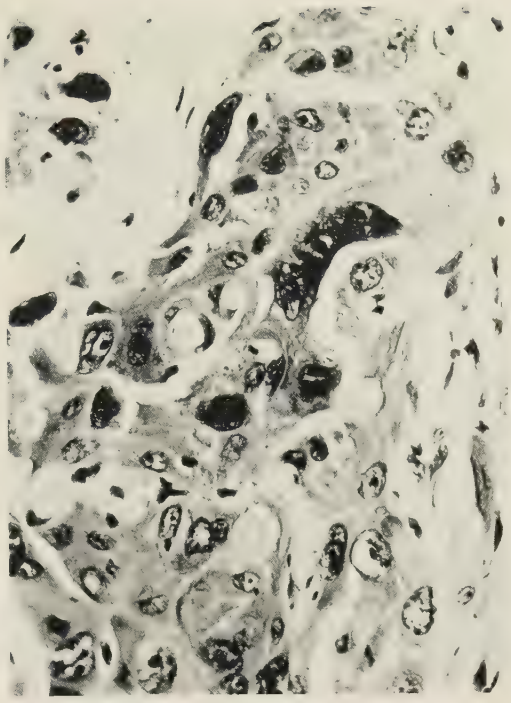

FIG. 127.

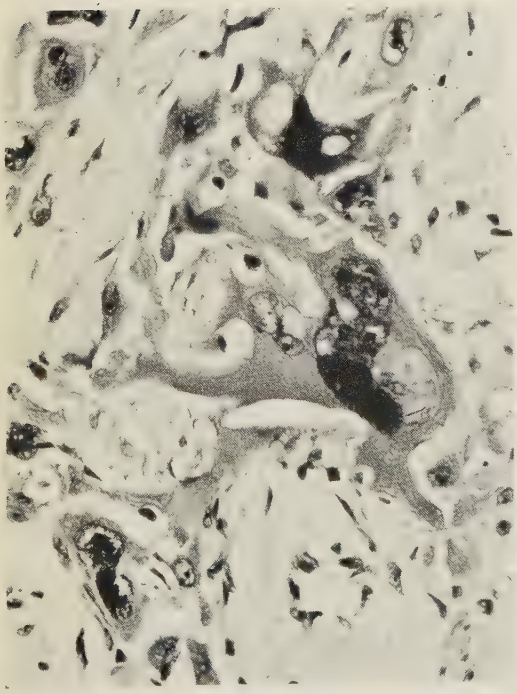

FIG. 128.

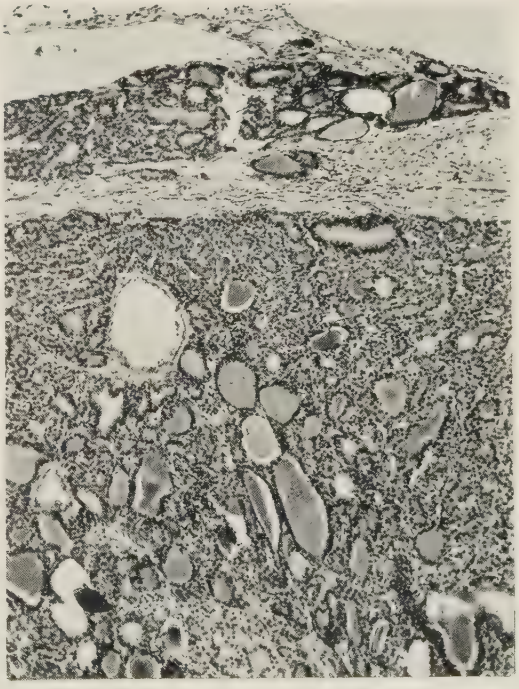

FIG. 129.

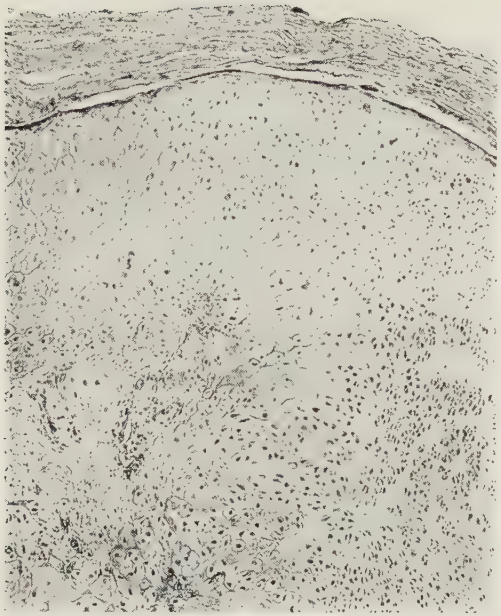

FIG. 130.

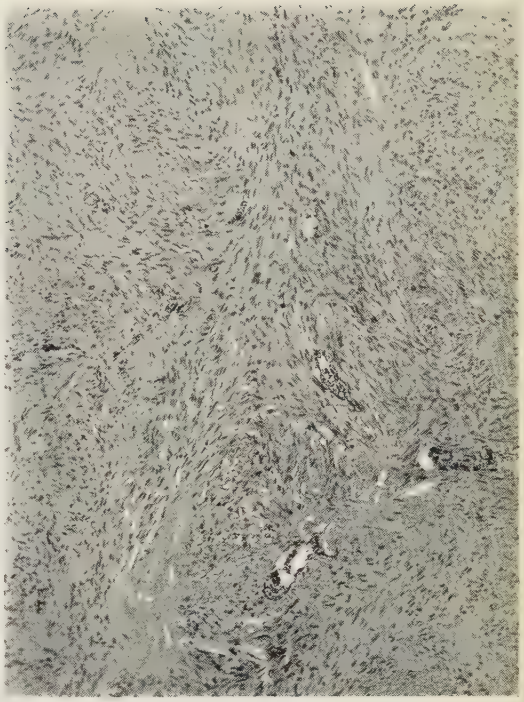

FIG. 131.

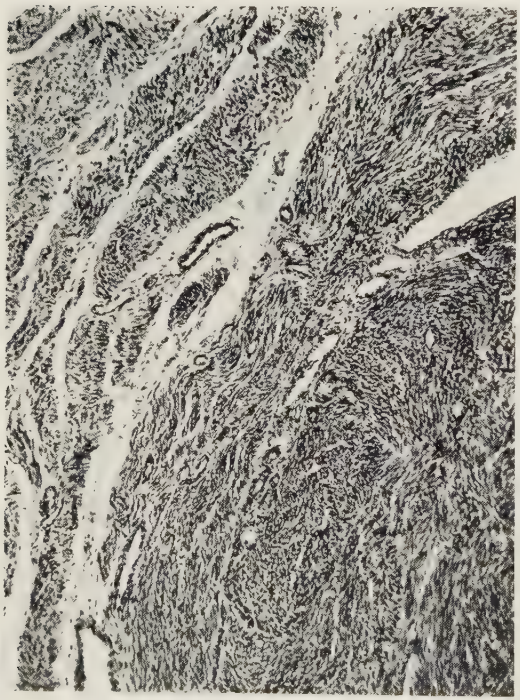

FIG. 132.

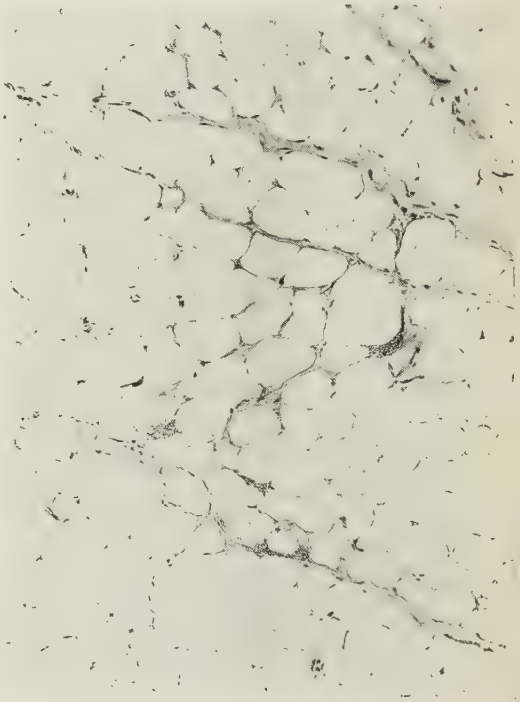

FIG. 133.

FIG. 130.—A chondroma showing its fibrous capsule, the irregular arrangement of the cells and their variation in size and shape.

FIG. 131.—A fibroma showing the interlacing bundles of dense fibrous tissue.

FIG. 132.—A myoma of uterus showing the richly nuclear interlacing muscle bundles, partly separated from the normal myometrium (on the left) by delicate fibrous tissue.

FIG. 133.—A lipoma showing its close resemblance to normal fatty tissue.

FIG. 134.—Large round-celled sarcoma arising in bone showing the closely packed cells and scanty protoplasm.

FIG. 135.—Spindle-celled sarcoma showing the variation in size and shape of the nuclei and the scanty fibre.

FIG. 136.—Another spindle-celled sarcoma showing rather more differentiation with the production of fibrous tissue. (A very cellular fibrosarcoma.)

FIG. 137.—Giant nuclei and large irregular cells in an unusual form of fibrosarcoma. The majority of the nuclei contain many prominent nucleoli.

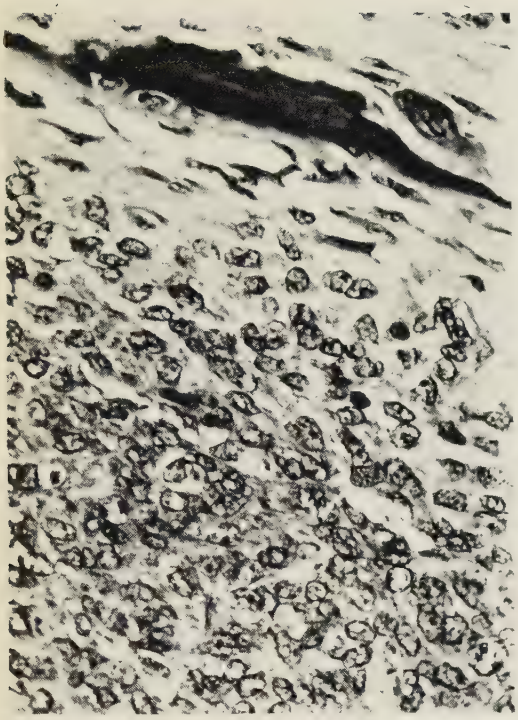

Fig. 134.

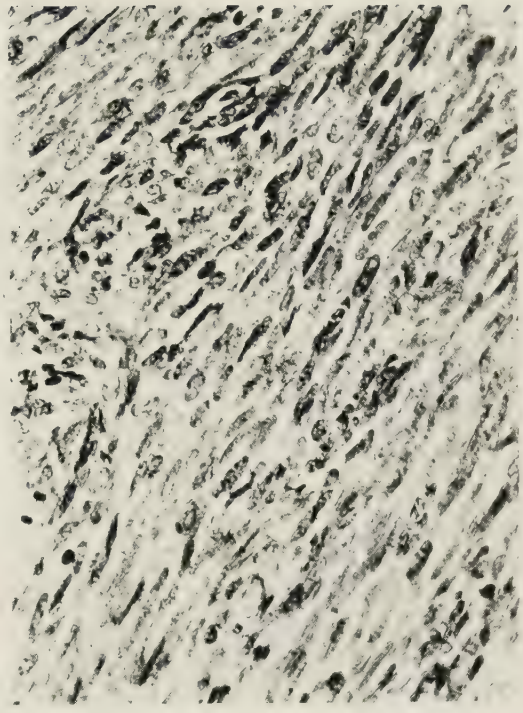

Fig. 135.

Fig. 136.

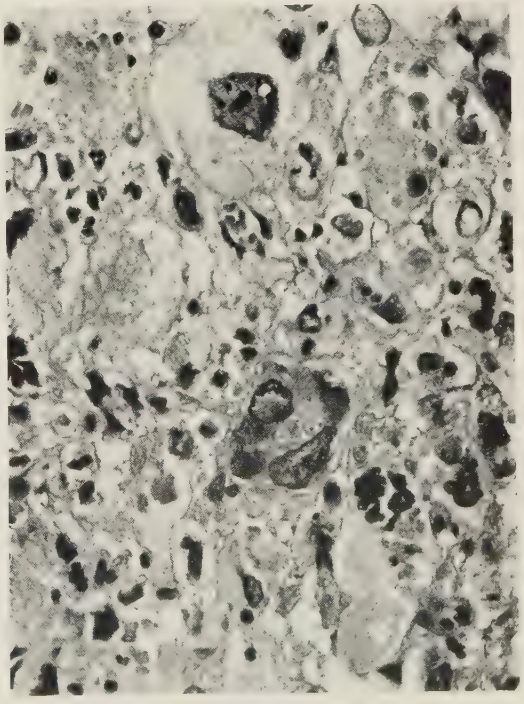

Fig. 137.

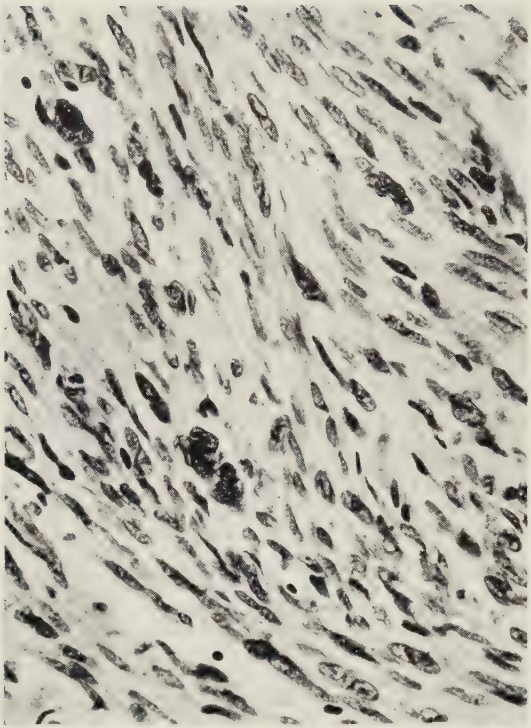

FIG. 138.

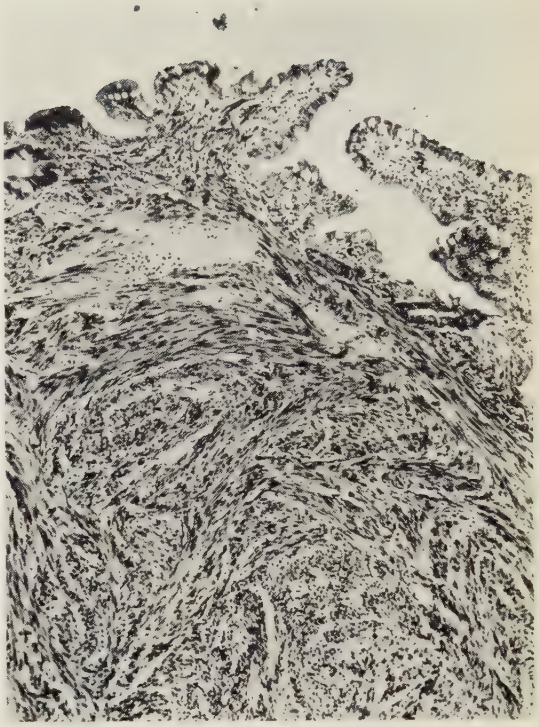

FIG. 139.

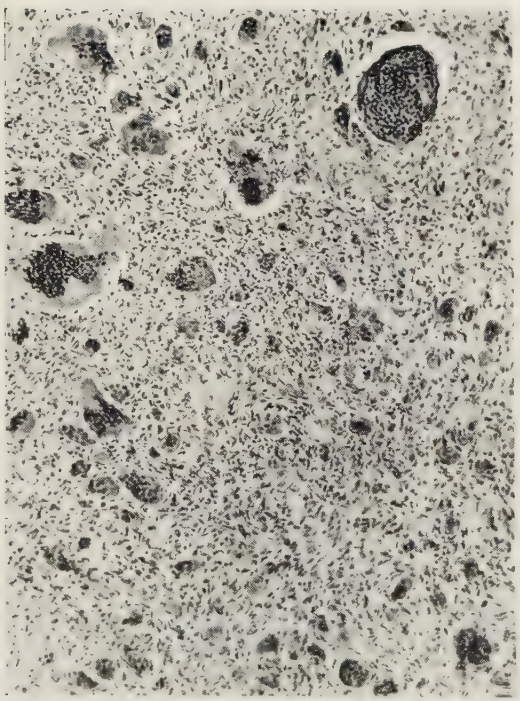

FIG. 140.

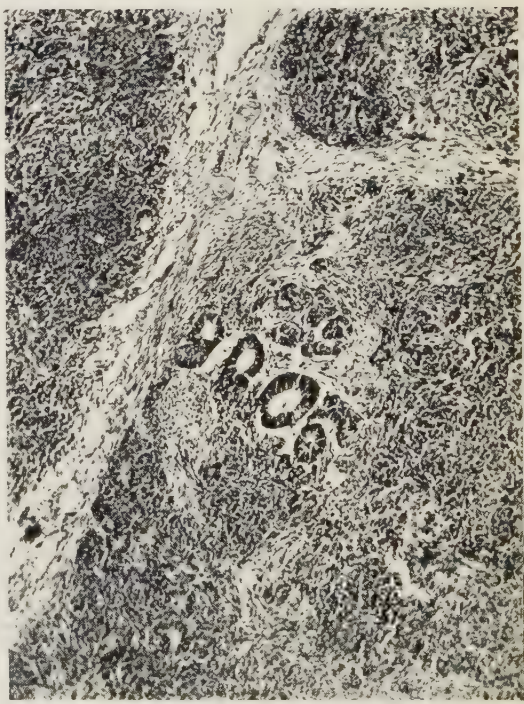

FIG. 141.

FIG. 138.—A myosarcoma of uterus showing the irregularity in size and shape of the cells and nuclei and two or three multinucleate giant cells.

FIG. 139.—Myosarcoma of small intestine infiltrating the submucosa and mucosa. The distortion of the mucosa and the bundles of muscles passing in all directions, quite unlike the muscle coats of normal intestine, are shown.

FIG. 140.—An osteoclastoma (myeloid sarcoma) showing the big and small irregular multinucleate giant cells and cellular fibrous tissue of which these tumours are composed. This tumour with few exceptions is only locally malignant.

FIG. 141.—A Wilm's tumour of kidney showing spindle-celled sarcoma and tubular, cubical and columnar-celled carcinoma. These tumours occur in young children, few having been described in children over three years of age. They are composed of all the elements which contribute to the formation of a kidney : the fibrous tissue may be represented by spindle cells, muscle or cartilage ; the epithelium by tubules lined by cubical or columnar cells, or by solid masses of epithelium. From their appearance, and the ages at which they occur, it would appear as if the malignant change takes place before differentiation has been completed, and instead of a kidney, a combined carcinoma and sarcoma is produced.

Angeiomata

ANGEIOMATA are of two kinds, one composed of blood-vessels called hæmangeiomata and the other of lymph vessels called lymphangeiomata. The former are the commoner and may arise in any part of the body. They are called capillary or cavernous, according to the size of the spaces they produce. In the skin and subcutaneous tissues they are especially common, and may be capillary, cavernous or both. They are also a common, accidental post-mortem finding in the liver, where they are most frequently multiple and cavernous.

FIG. 142.—A capillary and cavernous hæmangeioma (nævus) of skin showing the larger and smaller blood spaces in the subcutis.

FIG. 143.—A high-power view of a field taken from Fig. 142 showing the capillary part of the hæmangeioma. The closely packed capillaries, with walls of well-formed endothelial cells, some empty and others containing blood, are well shown. Between the capillaries a few endothelial cells can be seen.

FIG. 144.—A cavernous hæmangeioma of liver showing wide spaces containing blood and delicate fibrous walls lined by endothelium.

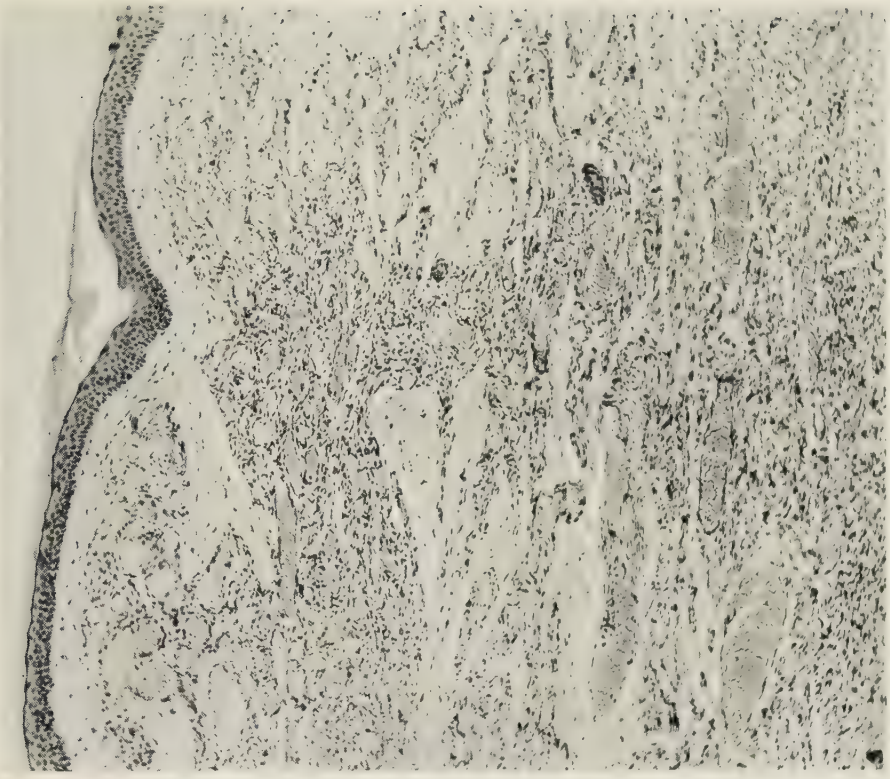

FIG. 142.

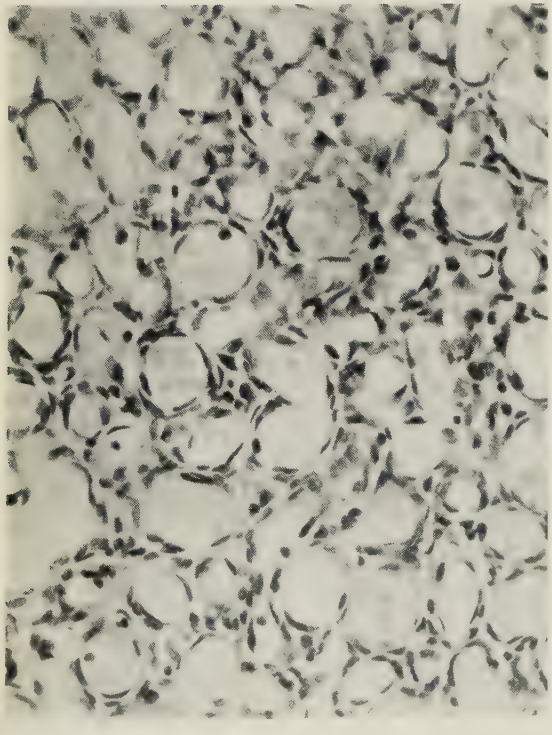

FIG. 143.

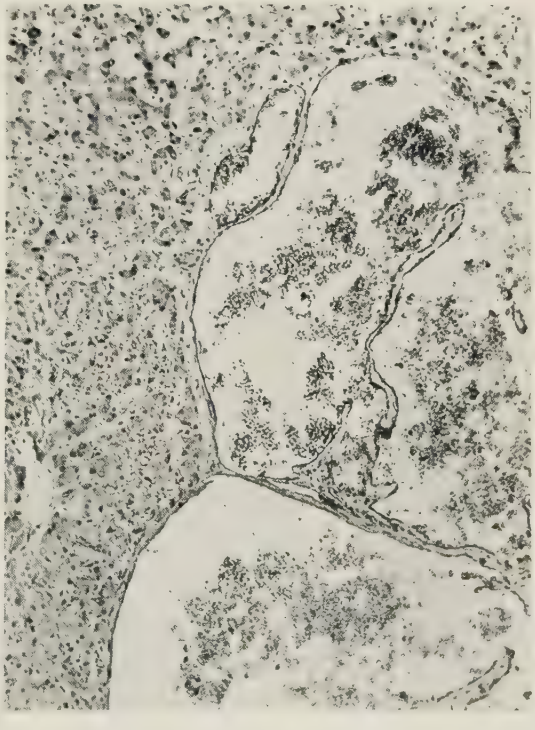

FIG. 144.

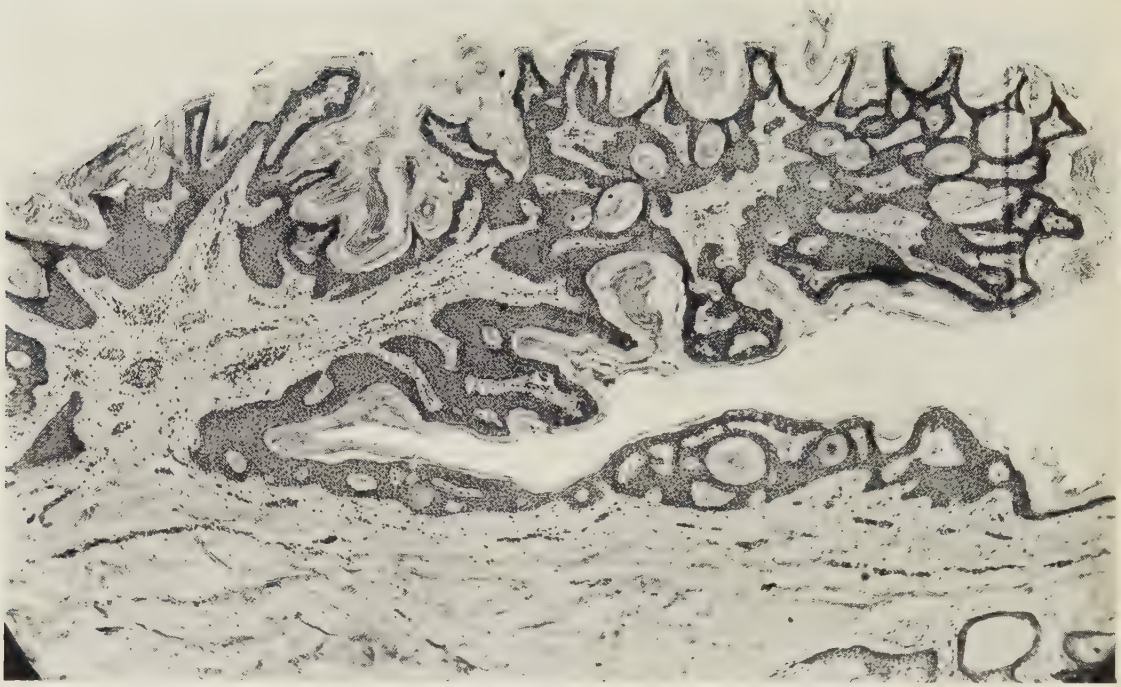

FIG. 145.

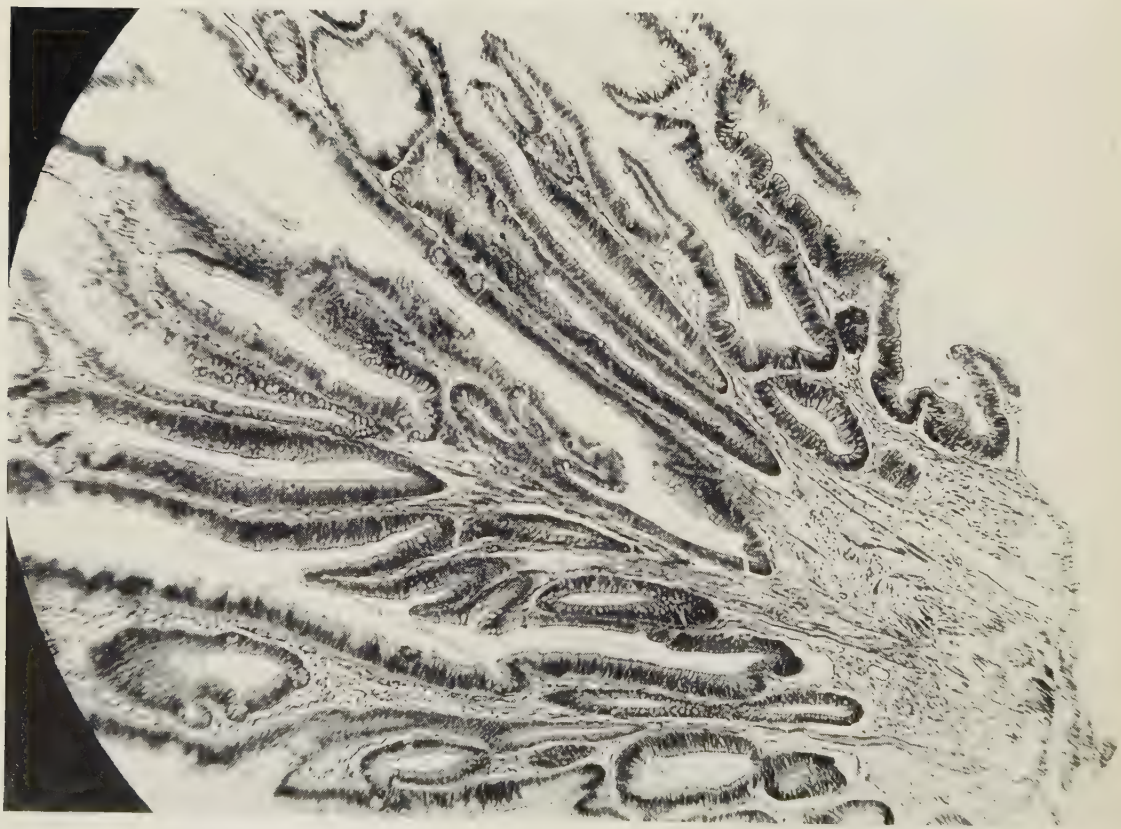

FIG. 146.

Papillomata

A PAPILLOMA is a benign newgrowth of epithelium growing in a branched or papillary form, in which each papilla has a central core of connective tissue containing blood-vessels. They are very common, and may arise from any surface covered by epithelium, including the inner surface of ducts or cysts.

FIG. 145.—A papilloma (wart) of skin. Its fibrous tissue core containing blood-vessels and its outgrowth from the surface are clearly seen.

FIG. 146.—A papilloma of rectum showing the columnar mucus-secreting epithelium, fibrous tissue core and projection from the surface.

FIG. 147.—A section showing a lactiferous duct and its opening on the nipple. The duct is distended by a profusely branching papilloma.

FIG. 148.—A low-power view of a branched papillary process, part of a papilloma of urinary bladder. It shows the central core, of scanty connective tissue and numerous blood-vessels, covered by transitional epithelium which form the delicate thread-like papillæ of which these tumours are composed.

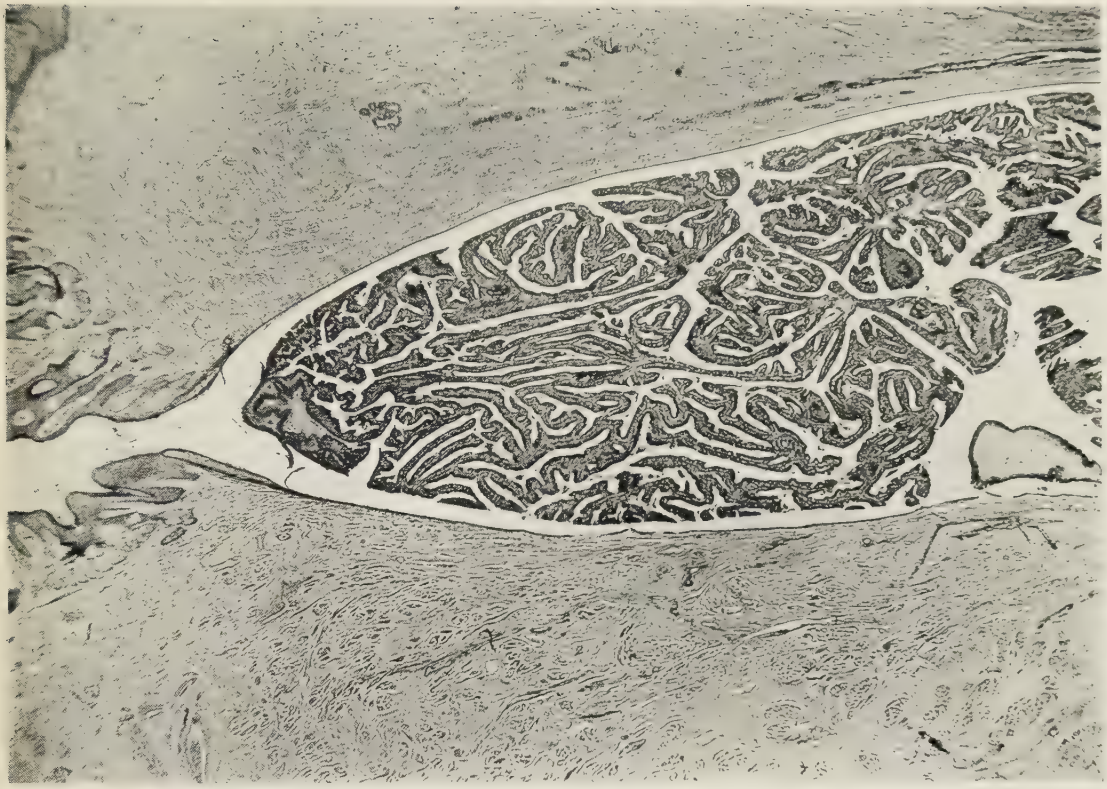

FIG. 147.

FIG. 148.

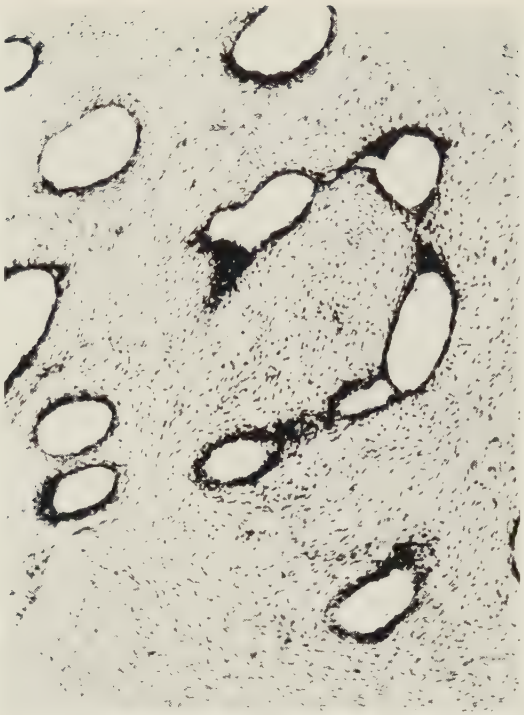

FIG. 149.

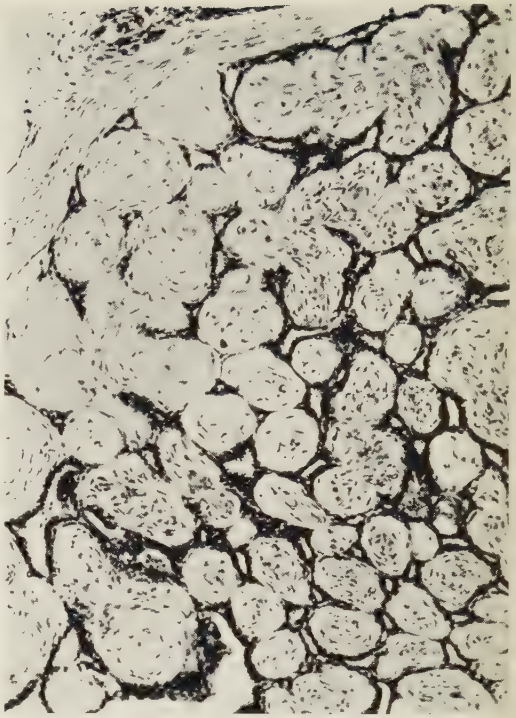

FIG. 150.

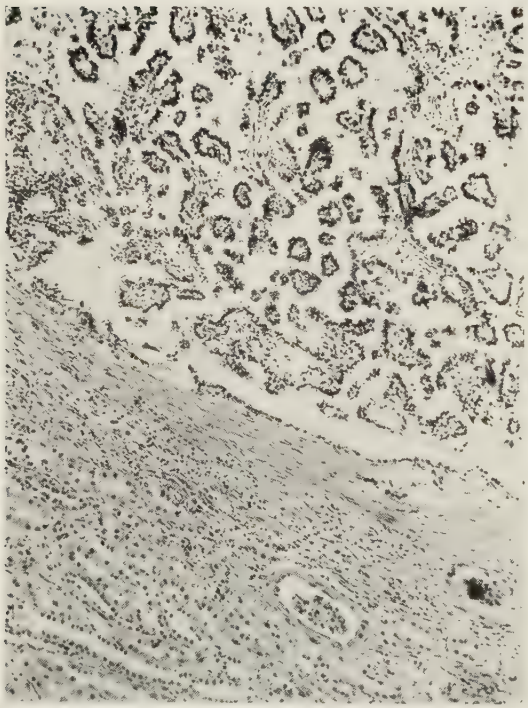

FIG. 151.

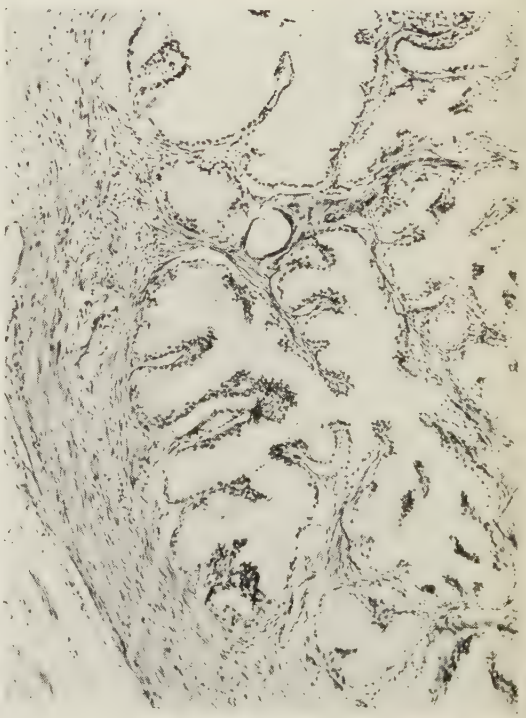

FIG. 152.

Adenomata

BENIGN newgrowths of glandular epithelium are called adenomata. They may arise in any glandular organ or surface covered by glandular epithelium, and are as varied in appearance as the tissue from which they grow. If with the glandular over-growth there is a similar growth of fibrous tissue the resulting tumour is called a fibro-adenoma, if of muscle a myoadenoma. When arising from a surface adenomata may be either polypoid (having a stalk) or sessile (without a stalk). In some situations adenomata often consist of a collection of cysts, and these are frequently wholly or partly filled by intracystic papillomata. One form of adenoma of kidney, for instance, is an intracystic papillary adenoma.

FIG. 149.—A fibro-adenoma of breast showing duct-like tubules surrounded by cellular fibrous tissue.

FIG. 150.—A fibro-adenoma of breast, in which the fibrous tissue has grown in an irregular manner so as to appear to be within the tubules. In most places in this specimen it can be clearly seen that the fibrous tissue is not within the lumen but merely bulging into the walls of the tubules.

FIG. 151.—An intracystic papillary adenoma of kidney showing the cysts almost filled by papillary growths.

FIG. 152.—A myoadenoma of prostate showing the glands and the smooth muscle in the trabeculæ.

Carcinomata

CARCINOMATA are malignant newgrowths arising in epithelium. The histological pictures which they present are infinitely varied, but do commonly conform to known types of epithelium, and this is used as the basis of most classifications.

A *rodent ulcer* is the least malignant of the carcinomata which arise from the squamous epithelium of the skin, and practically never gives rise to metastases. It may be ulcerated from the beginning or may at first project on the surface ; the older it is, however, the more likely is ulceration to take place. It grows slowly and infiltrates underlying tissues to an unlimited extent, even eroding and penetrating bone. The growth consists of solid masses and branching trabeculæ of cells, which in the central part are small and have oval deeply stained nuclei, while those in the periphery are taller and arranged as a palisade. The connective tissue surrounding the downgrowth is often myxomatous. Growths intermediate in malignancy and differentiation of cells, between rodent ulcers and squamous carcinoma, though not frequent, do occur.

A *squamous-celled carcinoma* is one which reproduces the characteristics of stratified squamous epithelium. Tumours of this type arise most frequently from skin, lip, tongue, œsophagus, cervix and other surfaces covered by similar epithelium. They do, however, arise less commonly from surfaces which are not normally lined by this type of epithelium. They may, or may not be, ulcerated, they burrow deep into the tissues and usually produce metastases in lymphatic glands and later in more distant organs such as lungs and liver.

The microscopic picture of these carcinomata shows solid masses and strands of squamous epithelium extending far down into the subepithelial tissues. Both the strands and masses are made up of cells corresponding to the basal, prickle and horny layers of normal skin. The basal layers are always in contact with the tissues they are infiltrating, so that strands in cross-section appear more or less circular, with central laminated horny layers surrounded by epithelium, and are called horny pearls or cell nests. Carcinomata arising from epithelium that does not normally develop a horny layer, such as that covering the œsophagus, may or may not produce horny pearls.

Adenocarcinomata.—These are carcinomata which reproduce glandular structure, and most commonly arise in glands, such as breast, stomach, colon, ovaries, gall-bladder, etc.

Papillary carcinoma is one which in addition to infiltrating tissues produces papillary processes.

Mucous (or colloid) carcinomata.—The cells of some carcinomata secrete mucus which, having no outlet, accumulates in the tumour, giving it a glistening macroscopic appearance somewhat like the cut surface of a thyroid. Some carcinomata of the thyroid produce colloid indistinguishable from that in a normal gland. The stroma of some carcinomata undergoes mucoid degeneration. These three different conditions are all grouped under the above heading.

Chorioncarcinoma.—This is an extremely interesting type of carcinoma which, arising in one individual, the fœtus, may infiltrate and destroy another, the mother ; it also emphasises the narrow border-line which separates physiological from pathological growth. The chorionic villi of the placenta (part of the fœtus) infiltrate the wall of the uterus and communicate with blood-vessels ; portions of them are sometimes carried to other parts of the body, and yet with the termination of pregnancy under normal conditions they all disappear. The villi consist of a central zone of myxomatous tissue and blood-vessels surrounded by two types of cell, an outer syncytial rim and an inner layer of cells of Langhans. The syncytium consists of protoplasm not divided into cells and contains scattered nuclei ; the Langhans' cells are fairly well defined, and have pale or clear protoplasm and round nuclei. Two pathological conditions may arise in connection with these villi : in one they become greatly swollen, œdematous and cyst-like (hydatidiform mole) ; in the other they take on the characters of a malignant growth (chorioncarcinoma). The malignancy of chorioncarcinomata varies within wide limits, removal by curettage being sufficient in some cases to effect a cure, while in others early widespread dissemination occurs. In the histological picture of these tumours both the syncytial and Langhans' cells are represented, though not arranged in the orderly manner of a normal villus. The growths are often very hæmorrhagic and associated with widespread infiltration of blood-vessels and large areas of necrosis.

FIG. 153.—A rodent ulcer showing the surface epithelium, which at the bottom right-hand corner is ulcerated, and the dark irregular masses and branching trabeculæ of cells infiltrating the subcutaneous tissue. The connective tissue between the masses and trabeculæ tends to be œdematous and to resemble myxomatous tissue.

FIG. 154.—A high-power view of the cell masses in a rodent ulcer showing the palisade of columnar cells in the periphery and the absence of differentiation of the cells in the central part.

FIG. 155.—A low-power view of a tumour which was characteristic of a rodent ulcer save for a few islands of cells in which there was some differentiation into prickle and horny layers. In the centre a poorly formed cell nest can be made out.

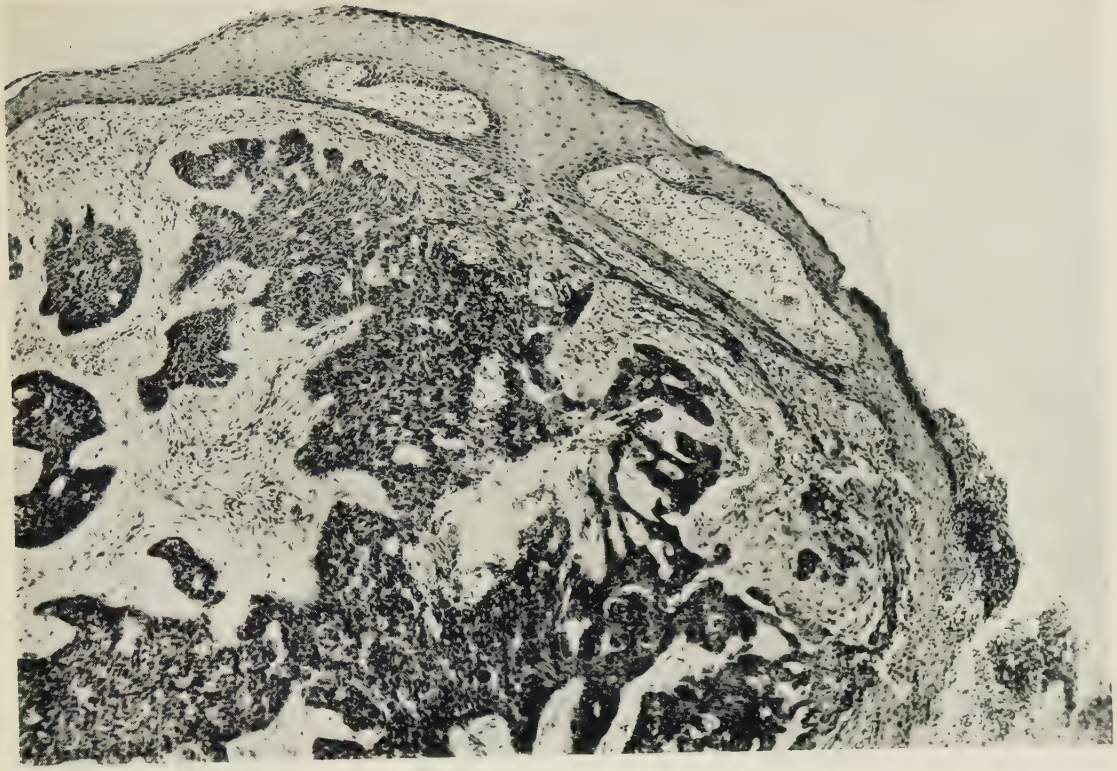

FIG 153.

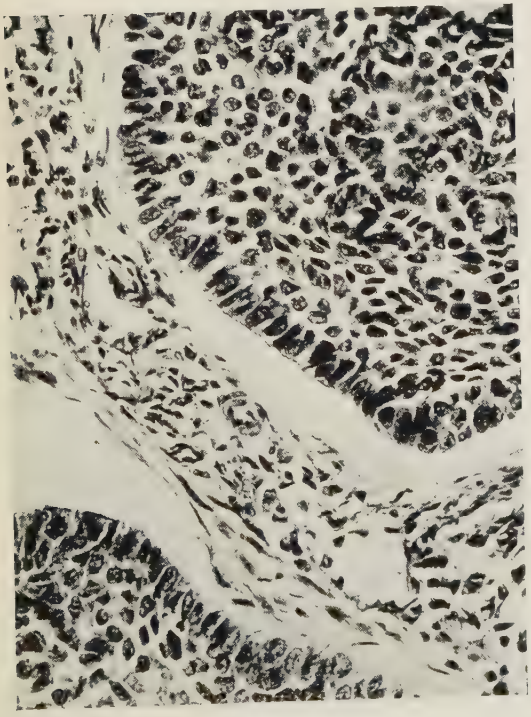

FIG. 154.

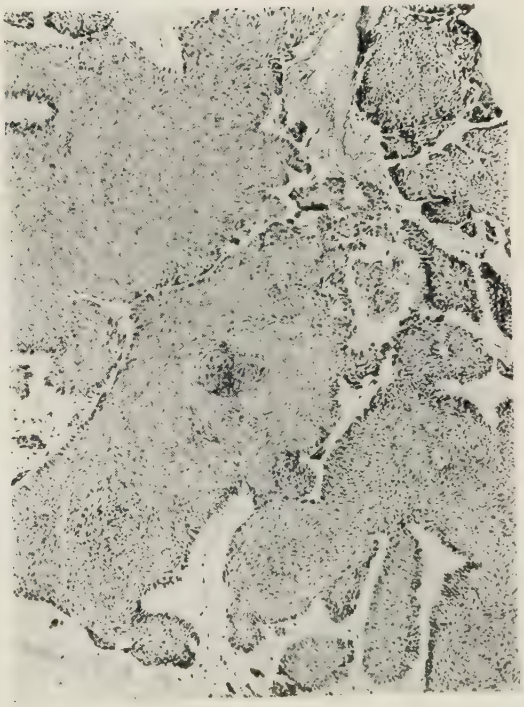

FIG. 155.

FIG. 156.

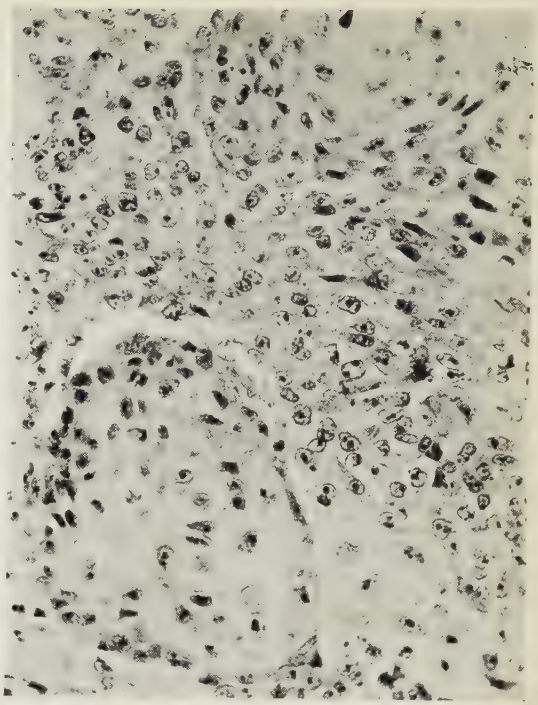

FIG. 157.

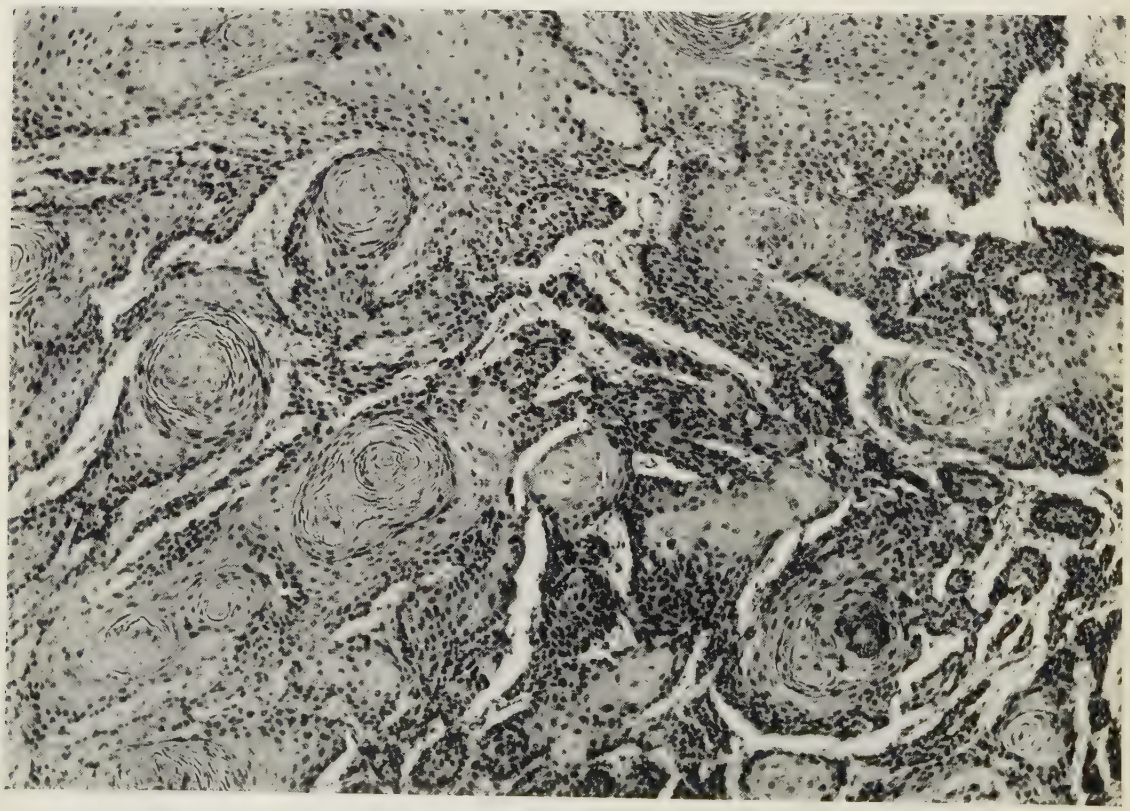

FIG. 158.

FIG. 156.—Squamous-celled carcinoma of skin, showing the irregular downgrowths extending into the subcutaneous tissues.

FIG. 157.—A squamous- and prickle-celled nodule in a carcinoma arising in pelvis of kidney. This is an example of metaplasia in a tumour, as the renal pelvis is normally lined by transitional epithelium.

FIG. 158.—A high-power view of squamous-celled carcinoma, showing the differentiation of the cells into basal, prickle and horny layers, with the production of cell nests or horny pearls.

FIG. 159.—A medullary or encephaloid carcinoma (of breast) showing the solid growth and absence of fibrous tissue. In the growth several mitotic figures can be seen.

FIG. 160.—A scirrhous carcinoma (of breast) showing the dense fibrous tissue and the small isolated islands of partly tubular cubical-celled and partly polygonal-celled carcinoma.

FIG. 161.—An intra-cystic papillary carcinoma of kidney (hypernephroma) showing the cysts and intra-cystic papillæ lined by very tall vacuolated columnar cells.

FIG. 162.—A solid trabecular and tubular cubical- and polygonal-celled carcinoma of prostate. Normal prostatic acini are seen at the top part of the figure.

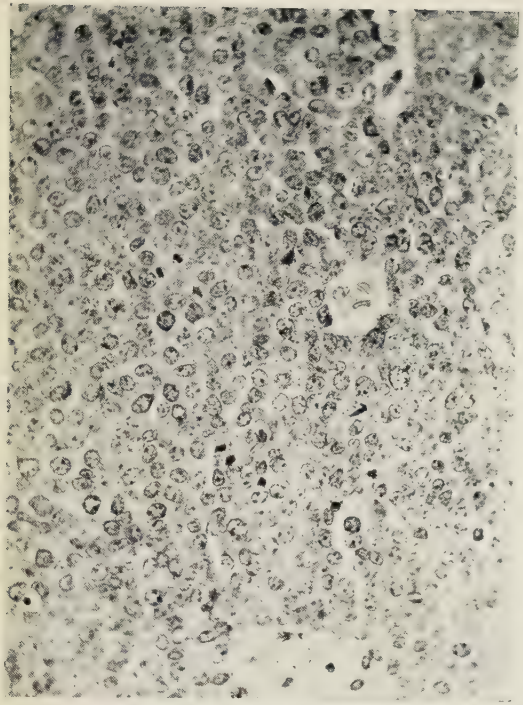

FIG. 159.

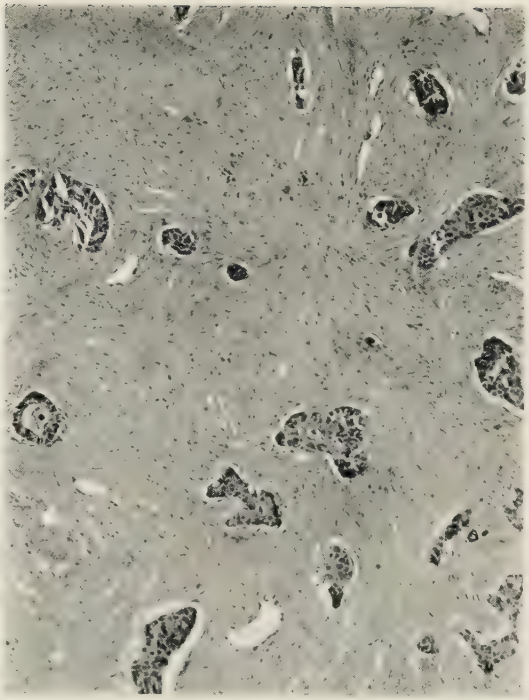

FIG. 160.

FIG. 161.

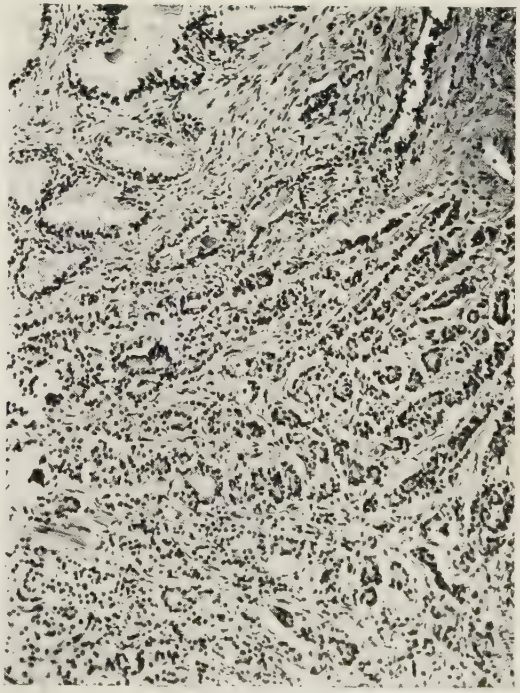

FIG. 162.

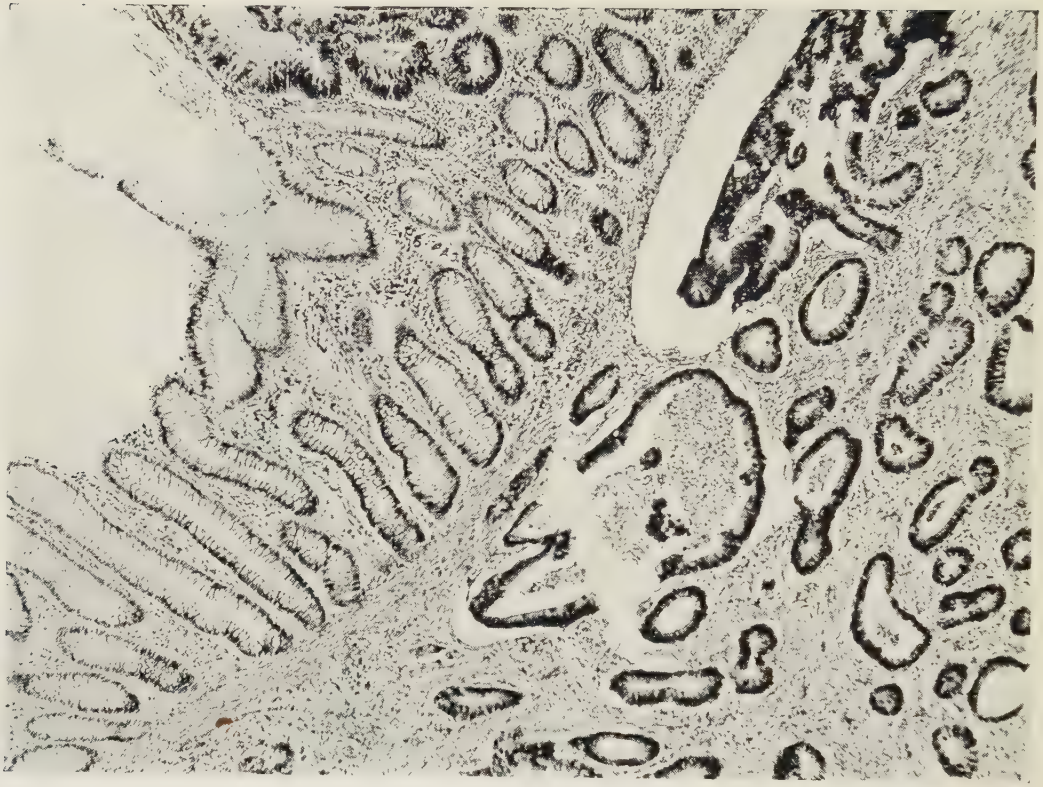

FIG. 163.

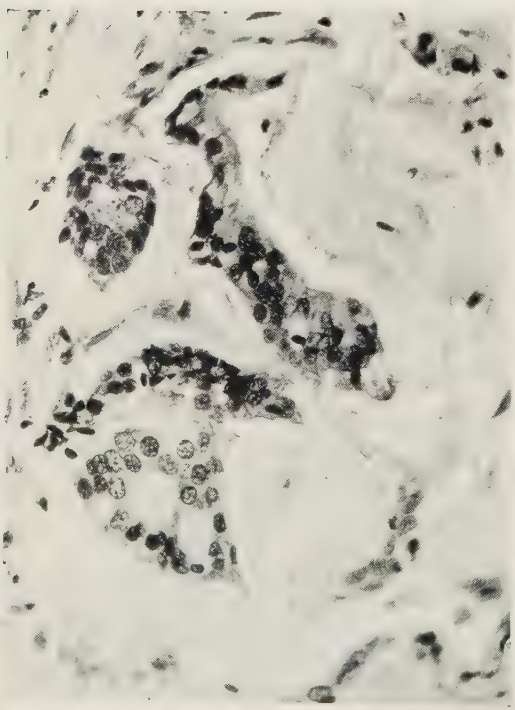

FIG. 164.

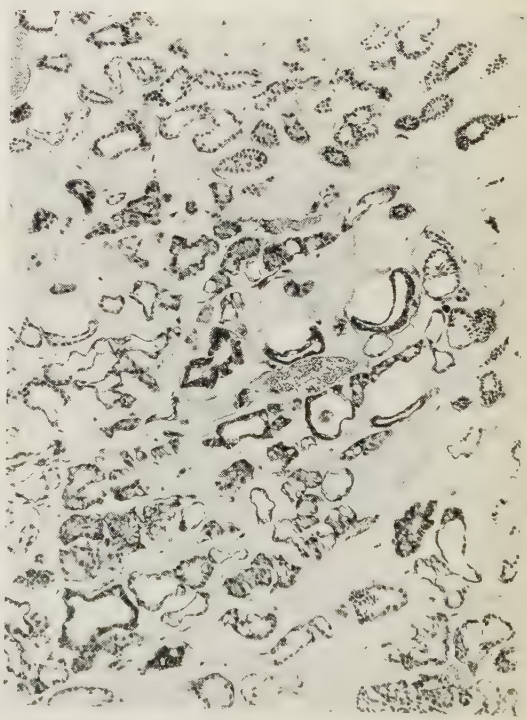

FIG. 165.

FIG. 163.—An adenocarcinoma of colon showing the junction of normal and carcinomatous mucous membrane and the infiltration of submucosa and muscularis.

FIG. 164.—A mucous carcinoma, showing a space filled with mucus and partly lined by columnar cells. The cells are not arranged in an orderly manner, and there are far too many nuclei for normal columnar epithelium.

FIG. 165.—A tubular cubical-celled carcinoma in which there is mucous degeneration of the stroma.

FIG. 166.—A general low-power view of chorioncarcinoma of uterus showing necrosed growth and groups of polygonal cells surrounded by narrow rims of syncytium in which are many deeply stained nuclei.

FIG. 167.—Syncytial masses with few vacuolated polygonal cells forming part of a chorioncarcinoma.

FIG. 168.—Vacuolated polygonal cells with well-formed nuclei and irregular syncytial masses with deeply stained nuclei in a chorioncarcinoma.

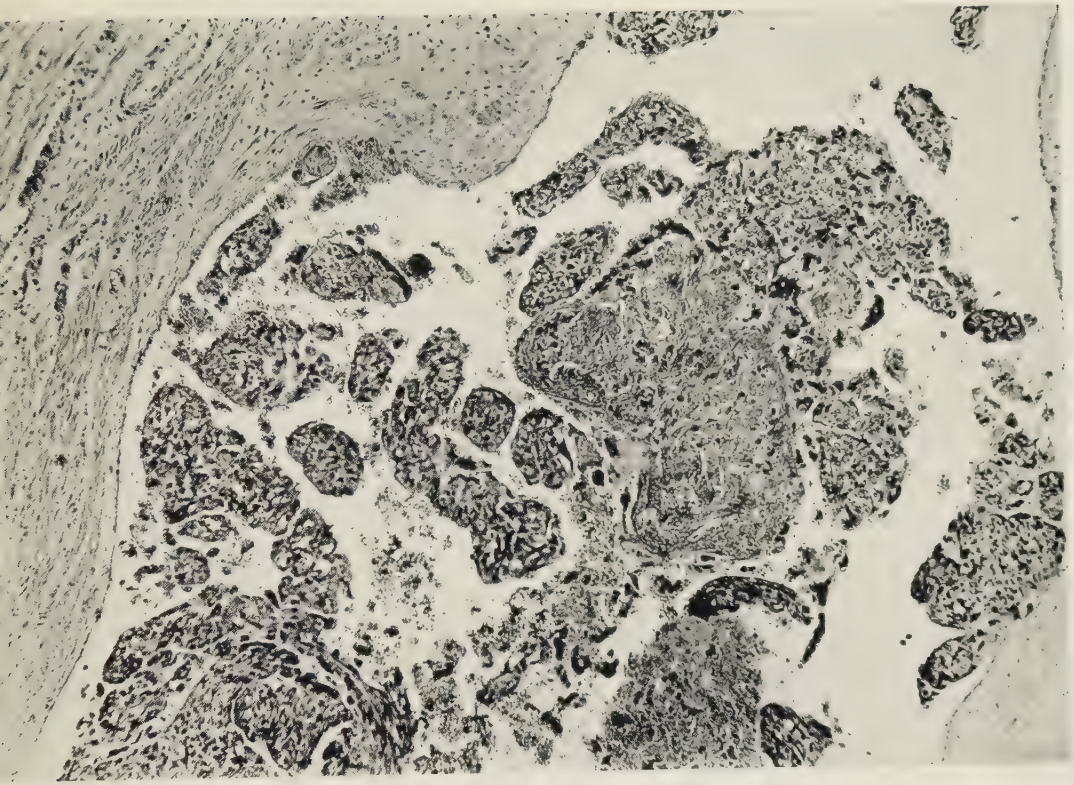

Fig. 166.

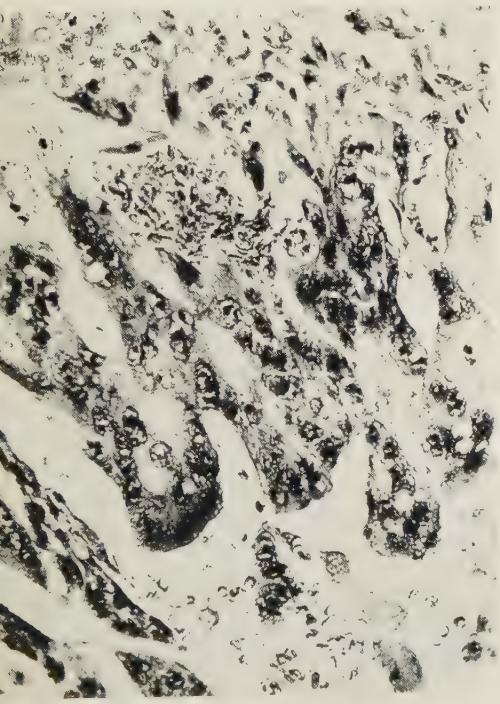

Fig. 167

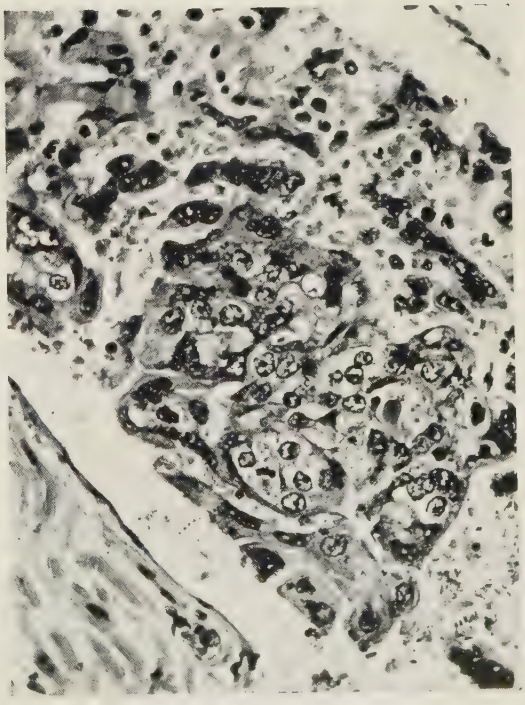

Fig. 168.

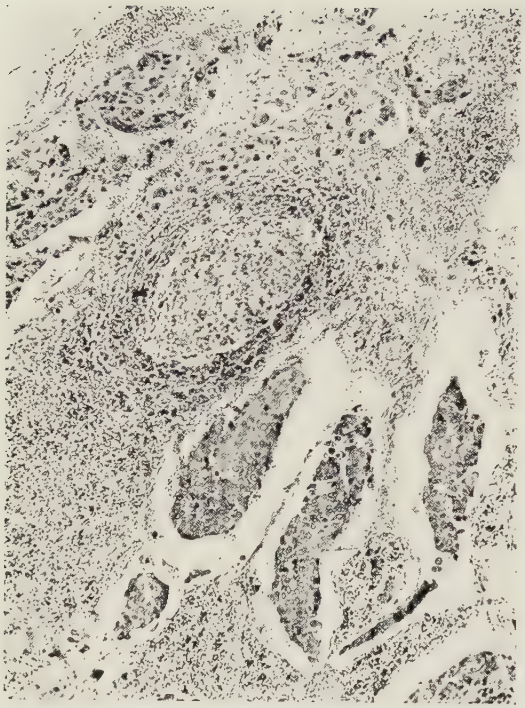

FIG. 169.

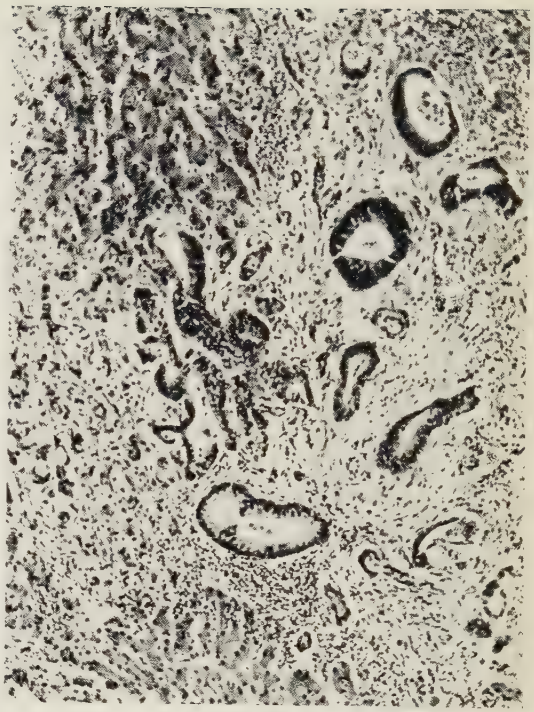

FIG. 170.

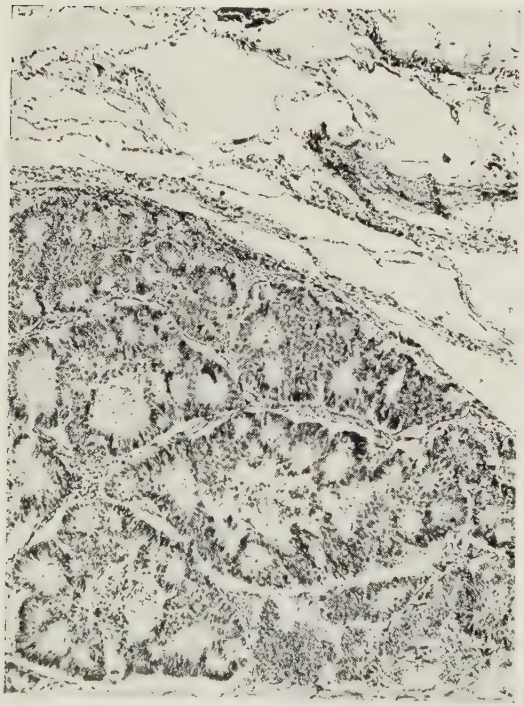

FIG. 171.

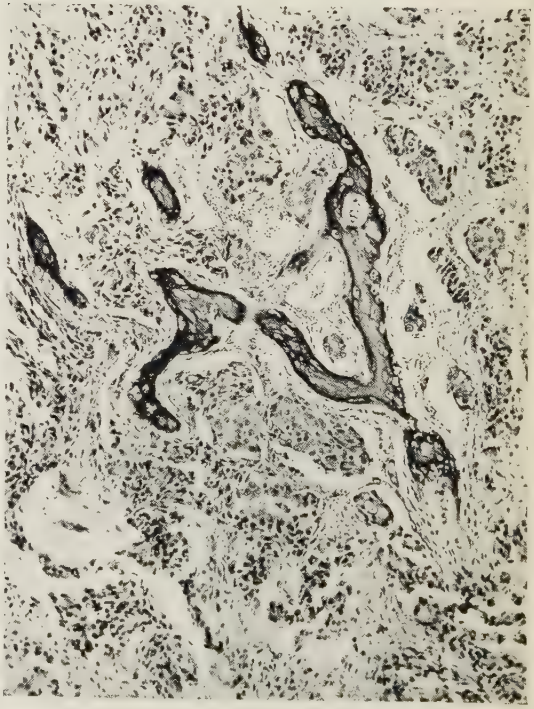

FIG. 172.

Metastases

SECONDARY growths usually bear a fairly close resemblance to the primary, but they do not necessarily do so. In some cases they are composed of better, in others of less, differentiated cells. Frequently scirrhous carcinomata, in which solid trabeculæ of polygonal cells are separated by wide zones of fibrous tissue, will produce tubular cubical-celled secondaries. Sometimes the secondaries from tubular cubical or columnar carcinoma will consist of a solid mass of polygonal cells. A secondary is, however, always composed of the same type of tissue as the primary, i.e. a squamous-celled carcinoma never gives rise to tubular secondaries. Carcinomata usually metastasise in lymphatic glands before doing so in other organs. Usually the glands affected are those which normally drain the part, but after that spread may take place against as well as with the lymph stream. After lymphatic glands the organs most commonly the seat of secondaries are liver, lung, bones, brain. Primary carcinomata of lung are often associated with very widespread dissemination, secondaries appearing in adrenals, kidneys and pancreas in addition to the organs mentioned above. The spleen is singularly free from secondary growths.

Secondary sarcoma may occur in lymphatic glands, but generally sarcomata infiltrate blood-vessels at an early stage and disseminate by the blood stream.

FIG. 169.—Secondary polygonal-celled carcinoma in lymphatic gland showing infiltration of subcapsular and deeper sinuses. (Primary in stomach.)

FIG. 170.—Secondary tubular columnar-celled scirrhous carcinoma in liver. (Primary in colon.)

FIG. 171.—Secondary tubular columnar-celled carcinoma in lung. In the lumen of the tubules remains of secretion and necrotic cells can be seen. (Primary in colon.)

FIG. 172.—Secondary polygonal-celled carcinoma in bone. (Primary in prostate.)

FIG. 173.—Secondary polygonal-celled carcinoma in the perivascular lymphatics in the lung.

FIG. 174.—A high-power view of a field taken from Fig. 173 showing the details of the polygonal cells.

FIG. 175.—Solid trabecular polygonal-celled carcinoma infiltrating lymphatic channels in fatty tissue in the neighbourhood of a lymphatic gland.

FIG. 176.—Secondary spindle-celled fibro-sarcoma in lung.

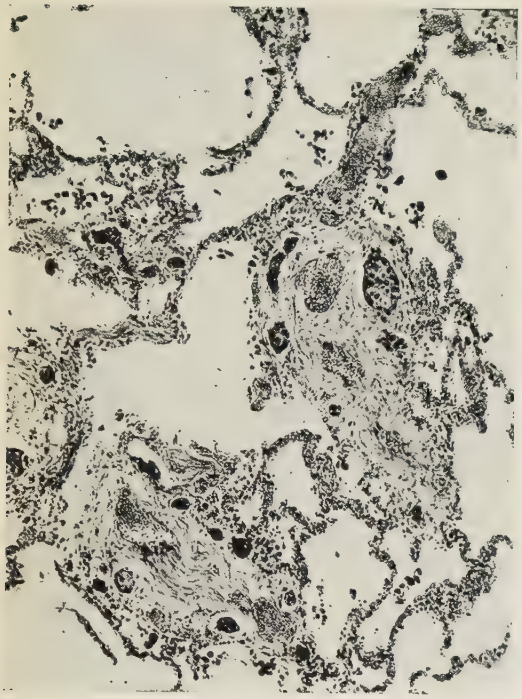

FIG. 173.

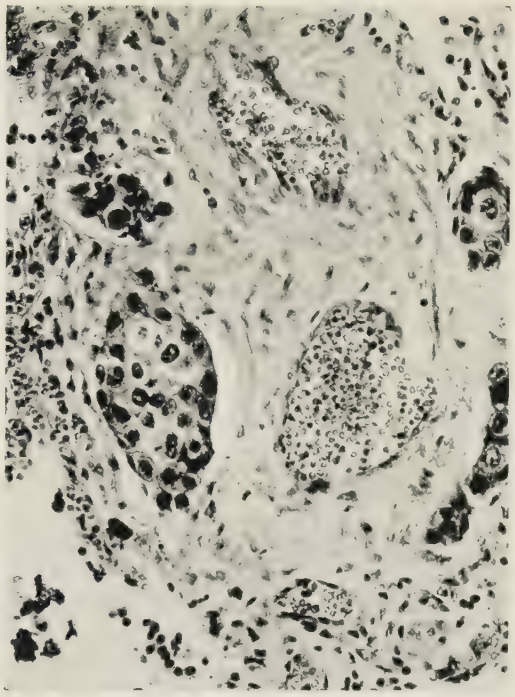

FIG. 174.

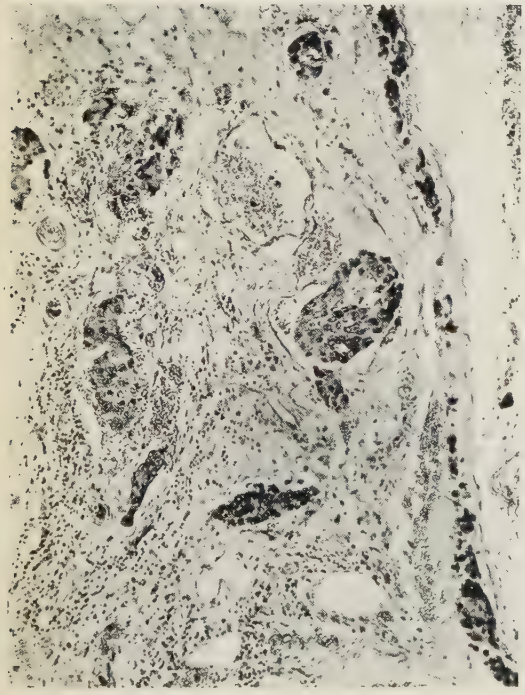

FIG. 175.

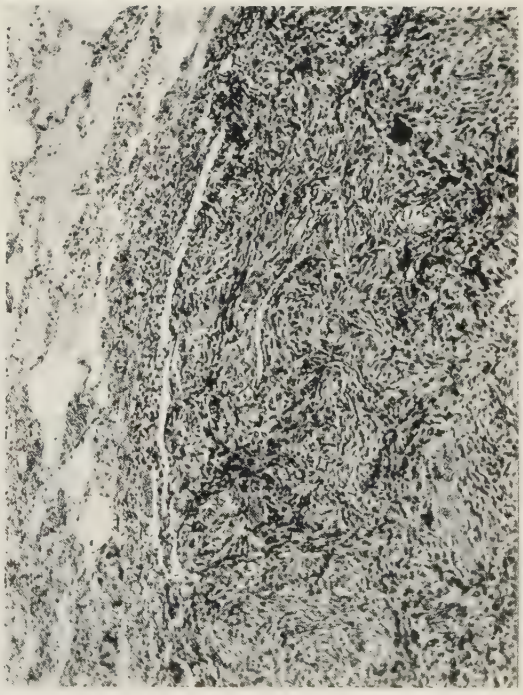

FIG. 176.